

10/608,101

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TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS	1	Web Page URLs for STN Seminar Schedule - N. America
NEWS	2	"Ask CAS" for self-help around the clock
NEWS	3	May 12 EXTEND option available in structure searching
NEWS	4	May 12 Polymer links for the POLYLINK command completed in REGISTRY
NEWS	5	May 27 New UPM (Update Code Maximum) field for more efficient patent SDIs in CApus
NEWS	6	May 27 CApus super roles and document types searchable in REGISTRY
NEWS	7	Jun 28 Additional enzyme-catalyzed reactions added to CASREACT
NEWS	8	Jun 28 ANTE, AQUALINE, BIOENG, CIVILENG, ENVIROENG, MECHENG, and WATER from CSA now available on STN(R)
NEWS	9	Jul 12 BEILSTEIN enhanced with new display and select options, resulting in a closer connection to BABS
NEWS	10	Jul 30 BEILSTEIN on STN workshop to be held August 24 in conjunction with the 228th ACS National Meeting
NEWS	11	AUG 02 IFIPAT/IFIUDB/IFICDB reloaded with new search and display fields
NEWS	12	AUG 02 CApus and CA patent records enhanced with European and Japan Patent Office Classifications
NEWS	13	AUG 02 STN User Update to be held August 22 in conjunction with the 228th ACS National Meeting
NEWS	14	AUG 02 The Analysis Edition of STN Express with Discover! (Version 7.01 for Windows) now available
NEWS	15	AUG 04 Pricing for the Save Answers for SciFinder Wizard within STN Express with Discover! will change September 1, 2004
NEWS EXPRESS		JULY 30 CURRENT WINDOWS VERSION IS V7.01, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
NEWS HOURS		STN Operating Hours Plus Help Desk Availability
NEWS INTER		General Internet Information
NEWS LOGIN		Welcome Banner and News Items
NEWS PHONE		Direct Dial and Telecommunication Network Access to STN
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Enter NEWS followed by the item number or name to see news on that specific topic.

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10/608,101

FILE 'HOME' ENTERED AT 18:29:32 ON 16 AUG 2004

=> file reg

COST IN U.S. DOLLARS

SINCE FILE
ENTRY

TOTAL
SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'REGISTRY' ENTERED AT 18:29:37 ON 16 AUG 2004

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Property values tagged with IC are from the ZIC/VINITI data file
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STRUCTURE FILE UPDATES: 15 AUG 2004 HIGHEST RN 727358-71-6

DICTIONARY FILE UPDATES: 15 AUG 2004 HIGHEST RN 727358-71-6

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

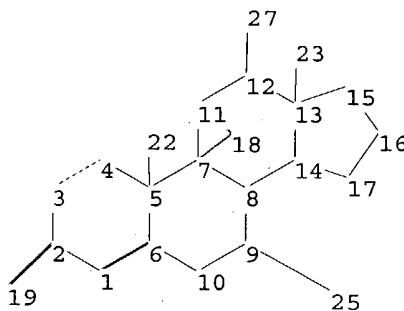
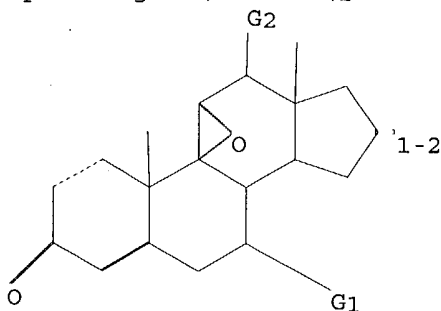
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:

<http://www.cas.org/ONLINE/DBSS/registryss.html>

=>

Uploading C:\STNEXP4\QUERIES\10608101.str



chain nodes :

19 22 23 25 27

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18

chain bonds :

2-19 5-22 9-25 12-27 13-23

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 7-11 7-18 8-9 8-14 9-10 11-12
11-18 12-13 13-14 13-15 14-17 15-16 16-17

exact/norm bonds :

1-2 1-6 2-3 2-19 3-4 4-5 5-6 5-7 6-10 7-8 7-11 7-18 8-9 8-14 9-10
9-25 11-12 11-18 12-13 12-27 13-14 13-15 14-17 15-16 16-17

exact bonds :

5-22 13-23

10/608,101

G1:C,O

G2:C,H,O,CN,X,Cb,Ak

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:CLASS
22:CLASS 23:CLASS 25:CLASS 27:CLASS

L1 STRUCTURE UPLOADED

=> s l1

SAMPLE SEARCH INITIATED 18:29:58 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 500 TO ITERATE

100.0% PROCESSED 500 ITERATIONS
SEARCH TIME: 00.00.01

2 ANSWERS

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**

PROJECTED ITERATIONS: 8659 TO 11341

PROJECTED ANSWERS: 2 TO 124

L2 2 SEA SSS SAM L1

=> d scan

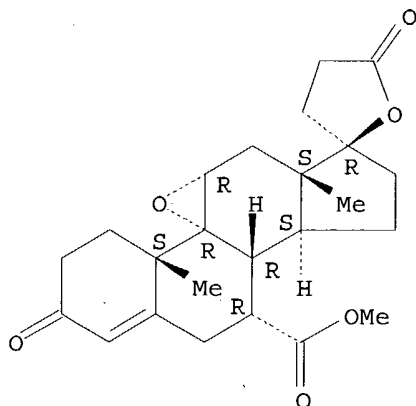
L2 2 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN

IN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with 1-butanol (9CI)

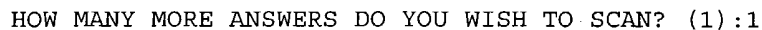
MF C24 H30 O6 . x C4 H10 O

CM 1

Absolute stereochemistry.



CM 2



CM 1

The chemical structure is a complex polycyclic molecule, likely a steroid derivative. It features a central core of fused rings. Key functional groups include a ketone group (C=O) on the left, a methyl group (Me) on the right, and a methoxy group (OMe) at the bottom. Stereochemistry is indicated with 'R' and 'S' labels and wedged/dashed bonds. A five-membered ring is attached to the top right, containing an oxygen atom and a carbonyl group.

CM 2



87 ANSWERS

SINCE	FILE	TOTAL
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10/608,101

	ENTRY	SESSION
FULL ESTIMATED COST	155.84	156.05

FILE 'CAPLUS' ENTERED AT 18:30:40 ON 16 AUG 2004
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FILE COVERS 1907 - 16 Aug 2004 VOL 141 ISS 8
FILE LAST UPDATED: 15 Aug 2004 (20040815/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> s l3
L4          158 L3

=> s l4 and 9, 11-epoxy steroid
    1695054 9
    841516 11
    210558 EPOXY
    2439 EPOXIES
    210853 EPOXY
        (EPOXY OR EPOXIES)
    102320 STEROID
    106860 STEROIDS
    157623 STEROID
        (STEROID OR STEROIDS)
    17 9, 11-EPOXY STEROID
        (9(W)11(W)EPOXY(W)STEROID)
L5          2 L4 AND 9, 11-EPOXY STEROID

=> s l4 and steroids
    106860 STEROIDS
L6          37 L4 AND STEROIDS

=> s l4 and 9, 11-epoxy
    1695054 9
    841516 11
    210558 EPOXY
    2439 EPOXIES
    210853 EPOXY
        (EPOXY OR EPOXIES)
    210 9, 11-EPOXY
        (9(W)11(W)EPOXY)
L7          6 L4 AND 9, 11-EPOXY

=> dup rem l5 l6 l7
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10/608,101

PROCESSING COMPLETED FOR L5

PROCESSING COMPLETED FOR L6

PROCESSING COMPLETED FOR L7

L8 38 DUP REM L5 L6 L7 (7 DUPLICATES REMOVED)

=> d 18 ibib hitstr abs 1-38

L8 ANSWER 1 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2004:220036 CAPLUS

DOCUMENT NUMBER: 140:247606

TITLE: Method to treat cardiac fibrosis with a combination therapy of an angiotensin II antagonist and an epoxy-steroidal aldosterone antagonist

INVENTOR(S): Egan, James J.; McMahon, Ellen G.; Olins, Gillian M.; Schuh, Joseph R.

PATENT ASSIGNEE(S): G.D. Searle & Co., USA

SOURCE: U.S. Pat. Appl. Publ., 146 pp., Cont.-in-part of U.S. Ser. No. 506,068, abandoned.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004053903	A1	20040318	US 2003-371699	20030221
PRIORITY APPLN. INFO.:			US 1997-783404	B1 19970113
			US 1997-980734	B3 19971201
			US 1998-181586	B1 19981028
			US 1999-317237	B1 19990524
			US 2000-506068	B1 20000217

OTHER SOURCE(S): MARPAT 140:247606

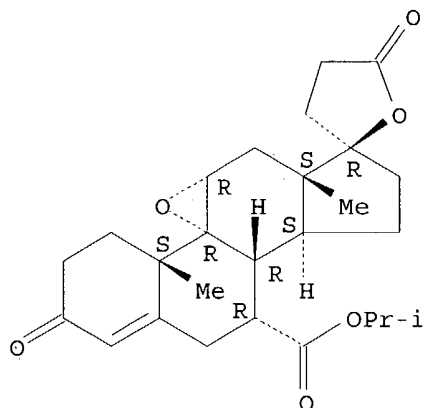
IT 95716-76-0, Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, 1-methylethyl ester, (7 α ,11 α ,17 α)- 95716-78-2, Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, ethyl ester, (7 α ,11 α ,17 α)- 95716-98-6, Pregn-4-ene-7,21-dicarboxylic acid, 9,11,-epoxy-17-hydroxy-3-oxo-, 7-methyl ester monopotassium salt, (7 α ,11 α ,17 α)- 95716-99-7, Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-(1-methylethyl) ester monopotassium salt, (7 α ,11 α ,17 α)- 95717-02-5, Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxodimethyl ester, (7 α ,11 α ,17 α)- 107724-20-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method to treat cardiac fibrosis and hypertrophy with a combination therapy of an angiotensin II (AngII) antagonist and an epoxy-steroidal aldosterone antagonist)

RN 95716-76-0 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, 1-methylethyl ester, (7 α ,11 α ,17 α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

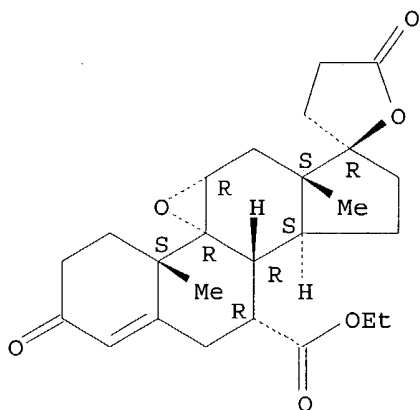
10/608,101



RN 95716-78-2 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ-lactone, ethyl ester, (7α,11α,17α)- (9CI) (CA
 INDEX NAME)

Absolute stereochemistry. Rotation (+).

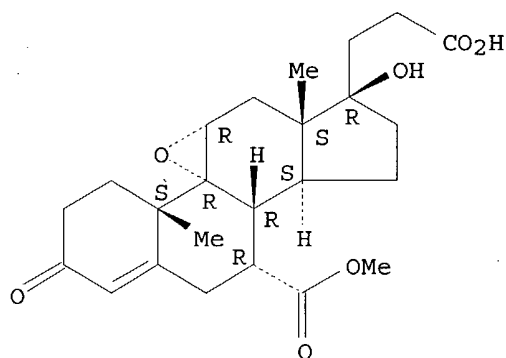


RN 95716-98-6 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-methyl ester, monopotassium salt, (7 α ,11 α ,17 α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10/608,101

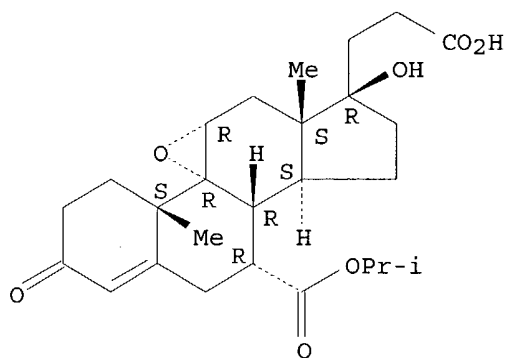


● K

RN 95716-99-7 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
7-(1-methylethyl) ester, monopotassium salt, (7 α ,11 α ,17 α) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



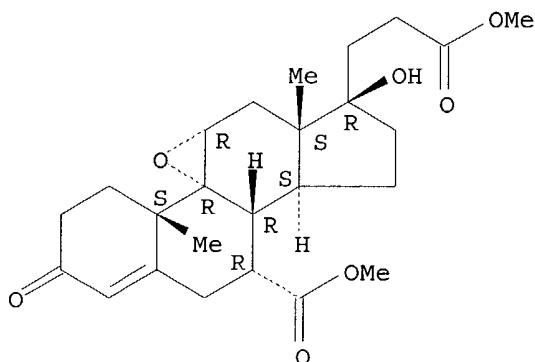
● K

RN 95717-02-5 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, dimethyl
ester, (7 α ,11 α ,17 α) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

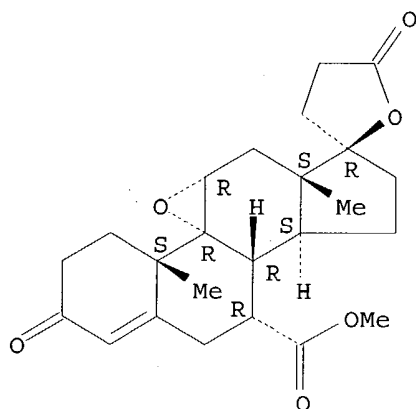
10/608,101



RN 107724-20-9 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



AB A therapeutic method is described for treating cardiac fibrosis or cardiac hypertrophy using a combination therapy comprising a therapeutically-effective amount of an epoxy-steroidal aldosterone receptor antagonist and a therapeutically-effective amount of an angiotensin II receptor antagonist. Preferred angiotensin II receptor antagonists are those compds. having high potency and bioavailability and which are characterized in having an imidazole or triazole moiety attached to a biphenylmethyl or pyridinyl/phenylmethyl moiety. Preferred epoxy-steroidal aldosterone receptor antagonists are 20-spiroxane steroidal compds. characterized by the presence of a 9α, 11α-substituted epoxy moiety. A preferred combination therapy includes the angiotensin II receptor antagonist 5-2-[5-[(3,5-dibutyl-1H-1,2,4-triazol-1-yl)methyl]-2-pyridinyl]phenyl-1H-tetrazole and the aldosterone receptor antagonist epoxymexrenone.

L8 ANSWER 2 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:182657 CAPLUS

DOCUMENT NUMBER: 140:210777

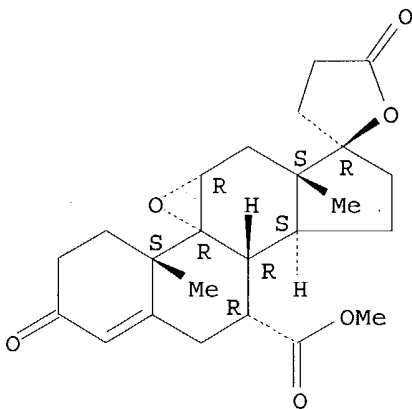
TITLE: Modulation of matrix metalloproteinase (MMP) activity
with eplerenone or other aldosterone blockers

10/608,101

INVENTOR(S): Rudolph, Amy E.; McMahon, Ellen G.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004017906	A2	20040304	WO 2003-US26251	20030822
WO 2004017906	A3	20040701		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004048840	A1	20040311	US 2003-645564	20030822
PRIORITY APPLN. INFO.:			US 2002-405292P	P 20020823
IT 107724-20-9, Eplerenone				
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)				
(modulation of matrix metalloproteinase (MMP) activity with eplerenone or other aldosterone blockers)				
RN 107724-20-9 CAPLUS				
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, methyl ester, (7 α ,11 α ,17 α)- (9CI) (CA INDEX NAME)				

Absolute stereochemistry.



AB The invention discloses a method for preventing an increase in matrix metalloproteinase (MMP) activity or reducing MMP activity in a subject in need thereof by administering to the subject a therapeutically effective amount of a selective aldosterone blocker. More particularly, the invention is directed to attenuating or preventing an increase in MMP activity

comprising administering eplerenone, or derivs. thereof. Therefore, the invention provides a method to treat patients who have symptoms of or have had symptoms of a condition selected from the group consisting of heart failure, renal disease, stroke, diabetes and syndrome X.

L8 ANSWER 3 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:414628 CAPLUS
DOCUMENT NUMBER: 140:423864
TITLE: Processes for preparing C-7 substituted
steroids from 5-androsten-3 β -ol-17-one
INVENTOR(S): Wuts, Peter Guillaume Marie
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 23 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004097475	A1	20040520	US 2003-392945	20030321
WO 2004043986	A1	20040527	WO 2003-US7284	20030321
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: US 2002-424488P P 20021107

OTHER SOURCE(S): CASREACT 140:423864; MARPAT 140:423864

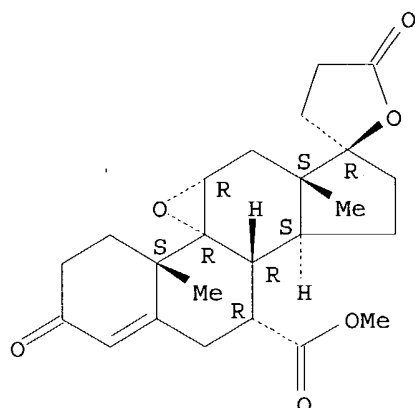
IT 107724-20-9P, Eplerenone

RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of C-7 substituted **steroids** from 5-androsten-3 β -ol-17-one)

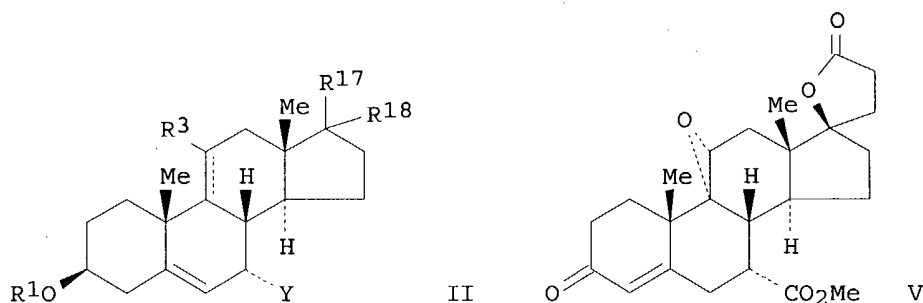
RN 107724-20-9 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



GI



AB The present invention discloses a process for the transformation of 5-androsten-3 β -ol-17-one (I) to C-7 substituted **steroids**, such as II [R1 = H, COR2; R2 = alkyl, alkoxy; R3 = H, OR1; R17R18 = O, lactone; Y = CN, CH2CH:CH2, 5-(C1-6-alkyl)-2-furyl, 1-(C1-6-alkyl)-2-pyrrolyl, CHR4C(O)aryl, CHR4C(O)alkyl, CHR4C(O)X-aryl, CHR4C(O)X-alkyl; R4 = alkyl, aryl; X = O, S, dashed bond = single bond or double bond]. Thus, bioconversion of I to 5-androsten-3 β ,7 β -diol-17-one (III) was performed using a submerged culture of *Diplodia gossypina* ATCC 20571. III was subsequently converted to 5-androsten-3 β ,7 β ,11 α -triol-17-one (IV) using a submerged culture of *Aspergillus ochraceus* ATCC 18500. IV can also be obtained from II using a submerged culture of *Absidia coerulea* ATCC 6647. These intermediates are useful in the preparation of eplerenone (V).

L8 ANSWER 4 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:372862 CAPLUS

DOCUMENT NUMBER: 140:391400

TITLE: Processes for preparing 7-carboxy substituted **steroids** and intermediates thereof from 3 β ,7 β ,11 α -trihydroxy-androst-5-en-17-one and other **steroids**

INVENTOR(S): Marie, Wuts Peter Guillaume

PATENT ASSIGNEE(S): USA

10/608,101

SOURCE: U.S. Pat. Appl. Publ., 25 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004087562	A1	20040506	US 2003-392956	20030321
WO 2004043987	A1	20040527	WO 2003-US7285	20030321
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2002-424102P P 20021106

OTHER SOURCE(S): CASREACT 140:391400; MARPAT 140:391400

IT 107724-20-9P, Eplerenone

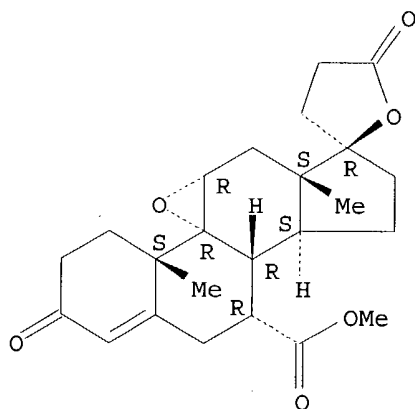
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of 7-carboxy substituted **steroids** and intermediates thereof from trihydroxyandrostene and other **steroids**)

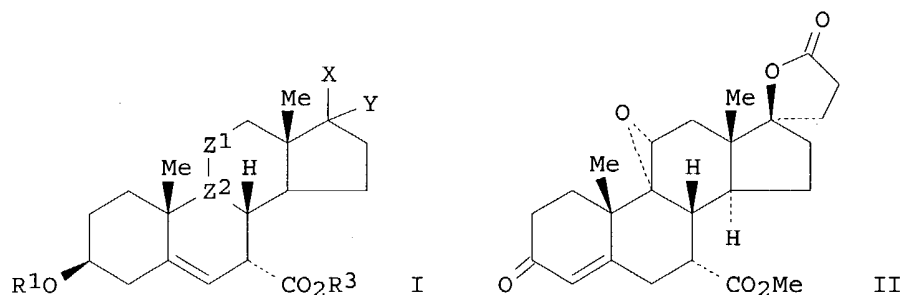
RN 107724-20-9 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, methyl ester, (7 α ,11 α ,17 α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



AB The present invention relates to processes for the preparation of 7-carboxy substituted steroid compds. and intermediates thereof, such as I [R1 = H, COR4 ; R3 = alkyl; R4 = alkyl, alkoxy; Z1 = CH2, CHOCOR4 (wherein OCOR4 is in the α configuration); Z2 = CH; Z1Z2= double bond; X = OH; Y = C.tplbond.CH; XY = :O, OCOCH2CH2; OCH(OH)CH2CH2]. Particularly, the invention is directed to novel and advantageous methods for the preparation of eplerenone (II). Thus, II was prepared via a multistep synthetic sequence starting from androst-5-en-3 β -ol-17-one.

L8 ANSWER 5 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2003:472394 CAPLUS

DOCUMENT NUMBER: 139:31256

TITLE: Methods and compositions for treating ophthalmic disorders with epoxy-steroidal aldosterone receptor antagonists

INVENTOR(S): Aiken, James W.

PATENT ASSIGNEE(S): Pharmacia Corporation, USA

SOURCE: PCT Int. Appl., 68 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003049745	A1	20030619	WO 2002-US39807	20021212
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

US 2003158162 A1 20030821 US 2002-317650 20021212

PRIORITY APPLN. INFO.: US 2001-341033P P 20011212

IT 95716-76-0 95716-78-2 95716-98-6

95716-99-7 95717-02-5 107724-20-9

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(methods and compns. for treating ophthalmic disorders with

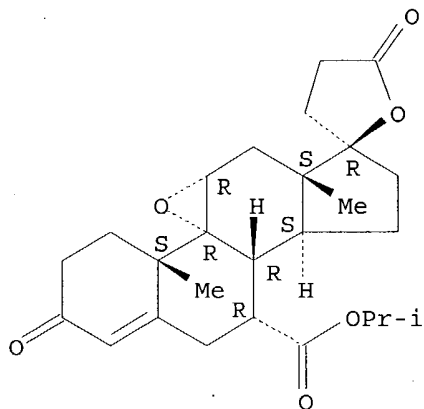
10/608,101

epoxy-steroidal aldosterone receptor antagonists)

RN 95716-76-0 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, 1-methylethyl ester, (7 α ,11 α ,17 α)-
(9CI) (CA INDEX NAME)

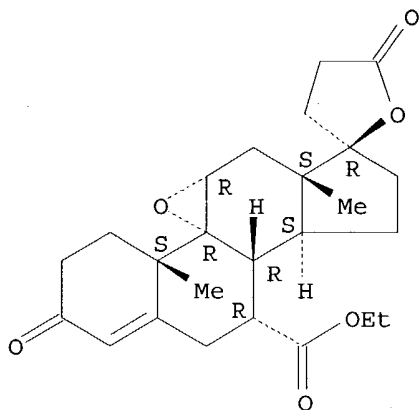
Absolute stereochemistry. Rotation (-).



RN 95716-78-2 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, ethyl ester, (7 α ,11 α ,17 α)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry. Rotation (+).

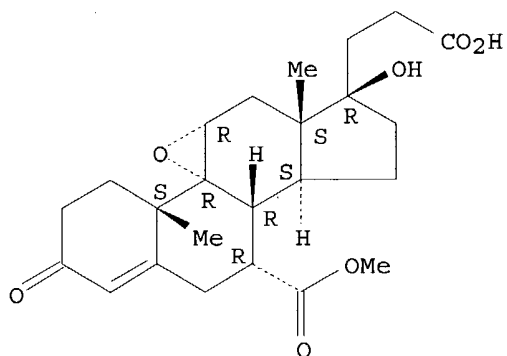


RN 95716-98-6 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-methyl
ester, monopotassium salt, (7 α ,11 α ,17 α)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

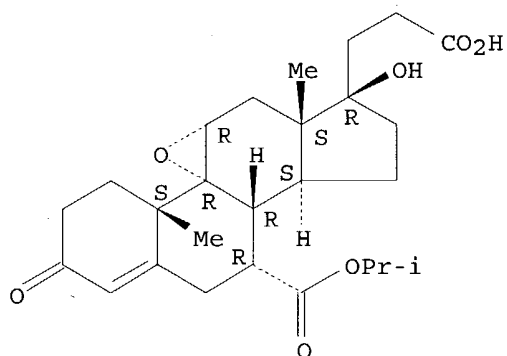
10/608,101



● K

RN 95716-99-7 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
7-(1-methylethyl) ester, monopotassium salt, (7 α ,11 α ,17 α) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

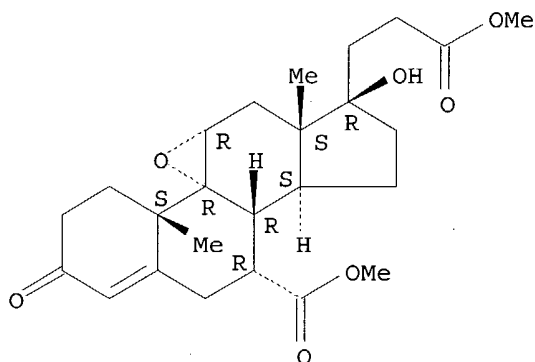


● K

RN 95717-02-5 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, dimethyl
ester, (7 α ,11 α ,17 α) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

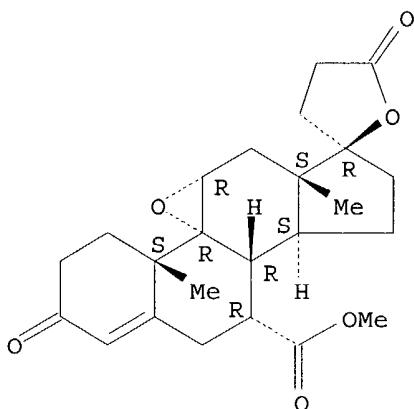
10/608,101



RN 107724-20-9 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



AB A method for treating or preventing ophthalmic disorders comprising the administration of one or more aldosterone receptor antagonists that contain a 9,11-epoxy moiety, such as eplerenone is disclosed. The method results in a reduction of intraocular pressure which treats or prevents the ophthalmic disorders. The epoxysteroid compds. can be co-administered with cytoskeletal disruptors, prostaglandin compds. and/or antiglaucoma agents. Among the disorders are intraocular hypertension, glaucoma, low tension glaucoma, age-related macula degeneration (AMD), macular edema, and diabetic retinopathy. As glucocorticoids and mineralocorticoids also cause the retention of ions, such as sodium and potassium, where aldosterone receptors are located, aldosterone receptor antagonists that contain a 9,11-epoxy moiety, such as eplerenone, also can be administered to modulate the intraocular concentration of ions. Thus, aldosterone receptor antagonists can be administered to maintain an intraocular ionic environment that is beneficial to intraocular cell survival.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:796726 CAPLUS

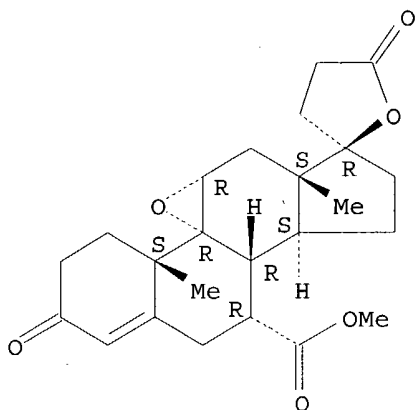
10/608,101

DOCUMENT NUMBER: 139:307925
TITLE: Process to prepare eplerenone and its intermediates from Δ^9 -canrenone and other pregnanes
INVENTOR(S): Pearlman, Bruce Allen; Padilla, Amphlett Greg; Havens, Jeffrey L.; Mackey, Sonja S.; Wu, Haifeng
PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA
SOURCE: PCT Int. Appl., 429 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003082895	A2	20031009	WO 2003-US7793	20030321
WO 2003082895	A3	20040422		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2003232981	A1	20031218	US 2003-392833	20030321
US 2004024202	A1	20040205	US 2003-392857	20030321
WO 2004037844	A1	20040506	WO 2003-US29923	20030919
WO 2004037844	C1	20040610		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2004127702	A1	20040701	US 2003-666175	20030919
PRIORITY APPLN. INFO.:			US 2002-366784P	P 20020322
			US 2002-411874P	P 20020919
			US 2002-425596P	P 20021112
			US 2003-392833	A 20030321
OTHER SOURCE(S):	CASREACT 139:307925; MARPAT 139:307925			
IT 107724-20-9P,	Eplerenone			
RL:	PNU (Preparation, unclassified); PREP (Preparation) (preparation of eplerenone and its intermediates from Δ^9 -canrenone and other pregnanes)			
RN 107724-20-9	CAPLUS			
CN	Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, methyl ester, (7 α ,11 α ,17 α)- (9CI) (CA INDEX NAME)			

Absolute stereochemistry.

10/608,101



IT 209253-82-7P

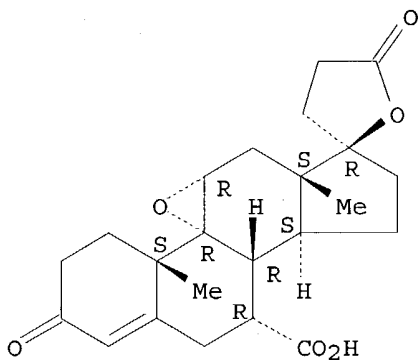
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of eplerenone and its intermediates from Δ^9 -canrenone and other pregnanes)

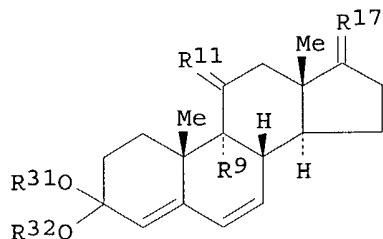
RN 209253-82-7 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, (7 α ,11 α ,17 α)- (9CI) (CA INDEX NAME)

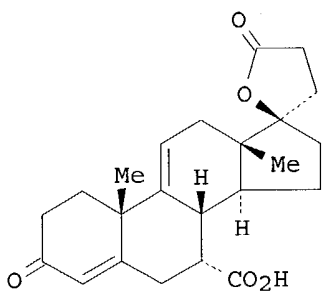
Absolute stereochemistry.



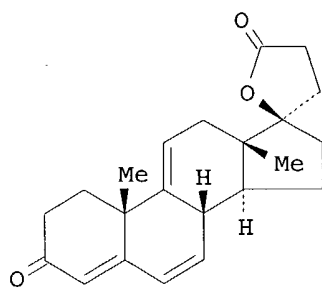
GI



I



II



III

AB The present invention involves novel intermediates I [R9 = H, OH, O-PG, F; PG = SiMe₃, SiEt₃, Ac, CHO; R11 = :O, H₂, αR11-1βR11-2, R11-5R11-6; R11-1 = H, OR11-3; R11-2 = H, OR11-4; R11-3 = H, PG; R11-4 = H, PG; R11-5R9 = bond, R11-6 = H or R11-6R9 = bond, R11-5 = H; R11-7R9 = O; R11-8 = H; R17 = :O, αR17-1βR17-2, αR17-3βR17-4, αR17-5βR17-6, αR17-7βR17-8, OCH(OR17-9)CH₂CH₂, αR17-11βR17-12; R17-1 = H, C.tplbond.CH, CN, C.tplbond.CCH₂αR17-1-1, C.tplbond.CCH₂O-PG, CH₂CH₂CO₂-; R17-2 = OH; R17-3 = OH; R17-4 = COMe, COCH₂OH, COCH₂OC(:O)(CH₂)O-3Me; R17-5R17-6 = α-CH₂O-β; R17-7R17-8 = α-OC(:O)CH₂CH₂-β; R17-9 = H, C1-3-alkyl; R17-11 = (CH₂)₁₋₂CH:CH₂; R17-12 = OH; R17-1-1 = H, Si(R17-1-2)₃; R17-1-2 = C1-4-alkyl, CH(OEt)Me, THP], including an 7α-substituted steroid, and various novel processes which are used to prepare known intermediates useful in the production of eplerenone, a pharmaceutical agent. Thus, pregnadienone spirolactone II was prepared from Δ⁹-canrenone (III) via conjugate addition of 2-methylfuran in MeNO₂ containing BF₃·OEt₂, ring cleavage with dibromantin in aqueous THF containing KOAc, ozonolysis (O₃/O₂) in CH₂Cl₂/O₂(CHMe₂)₂ with Me₂S quenching in CHCl₃ and oxidation in CHCl₃ with H₂O₂ in H₂O containing KHCO₃.

L8 ANSWER 7 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:796725 CAPLUS

DOCUMENT NUMBER: 139:307923

TITLE: C-17 spirolactonization and 6,7 oxidation of
steroids

INVENTOR(S): Miller, Paula C.; Pozzo, Mark J.; Chou, Shine K.

PATENT ASSIGNEE(S): Pharmacia Corporation, USA

SOURCE: PCT Int. Appl., 169 pp.

CODEN: PIXXD2

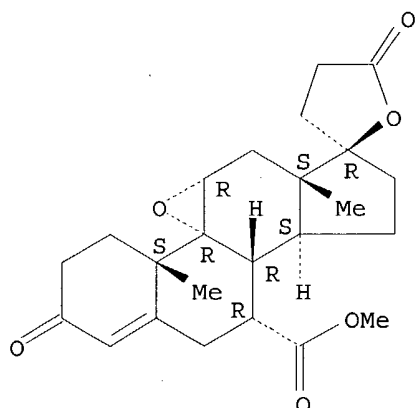
DOCUMENT TYPE: Patent

10/608,101

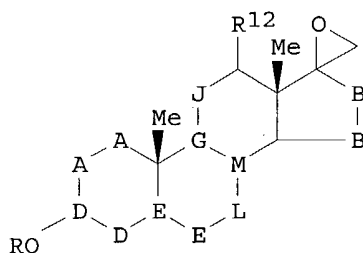
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003082894	A2	20031009	WO 2003-US7792	20030321
WO 2003082894	A3	20040415		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2003232981	A1	20031218	US 2003-392833	20030321
US 2004024202	A1	20040205	US 2003-392857	20030321
WO 2004037844	A1	20040506	WO 2003-US29923	20030919
WO 2004037844	C1	20040610		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2004127702	A1	20040701	US 2003-666175	20030919
PRIORITY APPLN. INFO.:			US 2002-366784P	P 20020322
			US 2002-411874P	P 20020919
			US 2002-425596P	P 20021112
			US 2003-392833	A 20030321
OTHER SOURCE(S):	CASREACT 139:307923; MARPAT 139:307923			
IT 107724-20-9P,	Eplerenone			
RL:	IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)			
	(C-17 spiro-lactonization and 6,7 oxidation of steroids)			
RN 107724-20-9	CAPLUS			
CN	Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, methyl ester, (7 α ,11 α ,17 α)- (9CI) (CA INDEX NAME)			

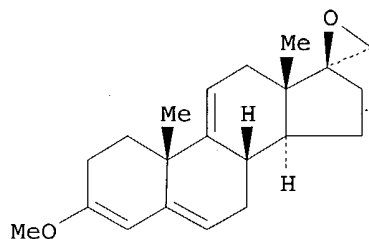
Absolute stereochemistry.



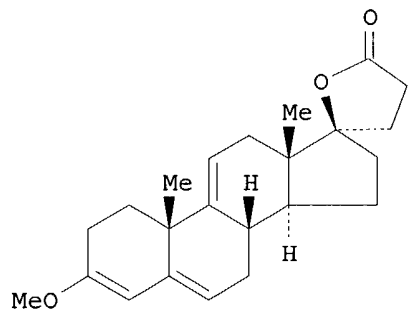
GI



I



II



III

AB The **steroids** I (R = alkyl; A-A = CHR1-CHR2, CR1=CR2; B-B = CHR15-CHR16; G-J = CR9-CHR11 or C=CR11; D-D = CH-CHR4, C=CR4; E-E = CH-CHR6 or C=CR6; L-M = CHR7-CH, CR7=C; R12, R1, R2, R15, R16, R9, R11, R4, R6, R7 = H, halo, OH, alkyl, alkoxy, acyl, HOCH2, alkoxyalkyl, hydroxycarbonyl, alkoxy carbonyl, acyloxyalkyl, cyano, nitro, thioalkyl, aryl, aryloxy) in prepared via processes for the C-17 spirolactonization and 6,7 oxidation of steroid compds. In certain preferred embodiments, the present invention provides for the preparation of steroid compds. which are useful in the preparation of Me hydrogen 9,11 α -epoxy-17 α -hydroxy-3-oxopregn-4-ene-7 α ,21-dicarboxylate γ -lactone (otherwise referred to as eplerenone or epoxymexrenone). Thus, treatment of 3-methoxyandrost-3,5,9(11)-trien-17-one with trimethylsulfonium methylsulfate in a reactor gave the oxirane derivative II, which reacted with

10/608,101

di-Et malonate followed by decarboxylation to give the lactone III, which was converted to $\Delta^9(11)$ -canrenone by an oxidation process using chloranil.

L8 ANSWER 8 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:777633 CAPLUS

DOCUMENT NUMBER: 139:281281

TITLE: Combination of an aldosterone receptor antagonist and a fibric acid derivative

INVENTOR(S): Keller, Bradley T.; McMahon, Ellen G.

PATENT ASSIGNEE(S): Pharmacia Corporation, USA

SOURCE: PCT Int. Appl., 80 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003080118	A2	20031002	WO 2003-US8206	20030318
WO 2003080118	A3	20040115		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: US 2002-365242P P 20020318

IT 107724-20-9, Eplerenone

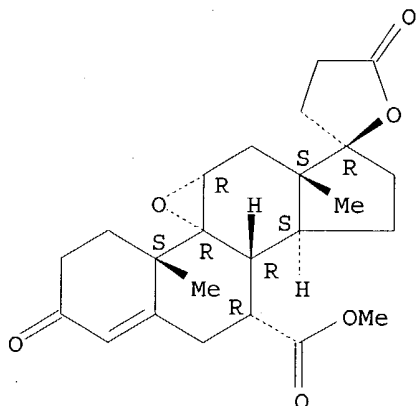
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(combination of aldosterone receptor antagonist and fibric acid derivative)

RN 107724-20-9 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, methyl ester, (7 α ,11 α ,17 α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB Novel methods and combinations for the treatment and/or prophylaxis of a pathol. condition in a subject, comprise the administration of 1 or more aldosterone receptor antagonists and 1 or more fibric acid derivs. and the combinations comprise 1 or more of the aldosterone receptor antagonists and the fibric acid derivs. Thus, a combination of eplerenone and gemfibrozil significantly increases the blood flow response to acetylcholine. Tablets contained eplerenone 25, gemfibrozil 300, lactose 54, microcryst. cellulose 15, HPMC 3, Croscarmellose sodium 2, and Mg stearate 1 mg.

L8 ANSWER 9 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:777601 CAPLUS

DOCUMENT NUMBER: 139:296974

TITLE: Combination of an aldosterone receptor antagonist and a bile acid sequestering agent

INVENTOR(S): Keller, Bradley T.; McMahon, Ellen G.

PATENT ASSIGNEE(S): Pharmacia Corporation, USA

SOURCE: PCT Int. Appl., 84 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003080069	A1	20031002	WO 2003-US8207	20030318
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003219401	A1	20031127	US 2003-391343	20030318
PRIORITY APPLN. INFO.:			US 2002-365390P	P 20020318
IT 107724-20-9, Eplerenone				
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL				

10/608,101

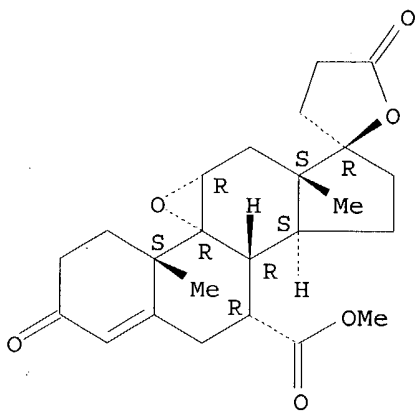
(Biological study); USES (Uses)

(combination of aldosterone receptor antagonist and bile acid sequestering agent)

RN 107724-20-9 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



AB Novel methods and combinations for the treatment and/or prophylaxis of a pathol. condition in a subject, comprise the administration of 1 or more aldosterone receptor antagonists and one or more, bile acid sequestering agents and the combinations comprise 1 or more of the aldosterone receptor antagonists and 1 or more of the bile acid sequestering agents. A combination of eplerenone and colestevlam significantly increases the forearm blood flow response to acetylcholine with an associated increase in vasoconstriction. Thus, tablets contained eplerenone 50, colestipol 2000, lactose 69.5, microcryst. cellulose 15, colloidal silica 0.5, talc 2.5, Croscarmellose sodium 2, and Mg stearate 0.5 mg.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:777600 CAPLUS

DOCUMENT NUMBER: 139:281278

TITLE: Combination of an aldosterone receptor antagonist and nicotinic acid or its derivatives

INVENTOR(S): Keller, Bradley T.; McMahon, Ellen G.; Krul, Elaine S.

PATENT ASSIGNEE(S): Pharmacia Corporation, USA

SOURCE: PCT Int. Appl., 85 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003080068	A1	20031002	WO 2003-US8201	20030318
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,				

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
 PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
 TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ,
 MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
 CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
 NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
 GW, ML, MR, NE, SN, TD, TG

US 2004067918 A1 20040408 US 2003-391212 20030318

PRIORITY APPLN. INFO.:

US 2002-365269P P 20020318

IT 107724-20-9, Eplerenone

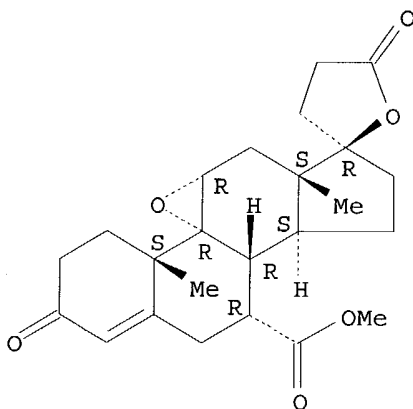
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)

(combination of aldosterone receptor antagonist and nicotinic acid or
 its derivs.)

RN 107724-20-9 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)- (9CI) (CA
 INDEX NAME)

Absolute stereochemistry.



AB Novel methods and combinations for the treatment and/or prophylaxis of a
 pathol. condition in a subject comprise the administration of 1 or more
 aldosterone receptor antagonists and 1 or more, nicotinic acid derivs. and
 the combinations comprise 1 or more of the aldosterone receptor
 antagonists and 1 or more of the nicotinic acid derivs. Thus, a tablet
 contained eplerenone 100, niacin 250, lactose 54, microcryst. cellulose
 15, HPMC 3, Croscarmellose sodium 2, and Mg stearate 1 mg. A combination
 of eplerenone and niacin improves the endothelial function.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 11 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:610301 CAPLUS

DOCUMENT NUMBER: 139:159932

TITLE: Aldosterone antagonist and nonsteroidal
 antiinflammatory agent combination therapy to prevent
 or treat cardiovascular disorders and
 inflammation-related disorders

INVENTOR(S): McMahan, Ellen G.; Rocha, Ricardo

PATENT ASSIGNEE(S): Pharmacia Corporation, USA

SOURCE: PCT Int. Appl., 158 pp.

10/608,101

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003063908	A1	20030807	WO 2003-US2923	20030130
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: US 2002-353008P P 20020130

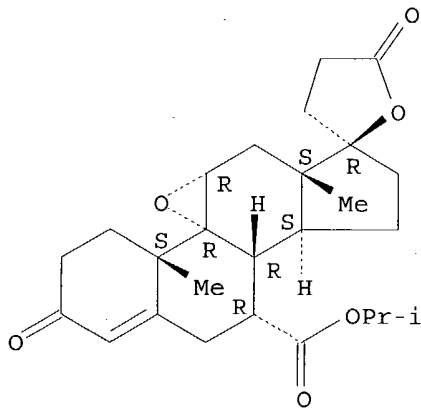
IT 95716-76-0 95716-78-2 95716-98-6
95716-99-7 95717-02-5 107724-20-9, Eplerenone
573652-78-5 573652-79-6 573652-80-9
573652-81-0 573652-82-1 573652-83-2
573652-84-3 573652-85-4 573652-86-5
573652-87-6 573652-88-7 573652-89-8
573652-90-1 573652-91-2 573652-92-3
573652-93-4 573652-94-5 573652-95-6
573652-96-7 573652-97-8 573652-98-9
573652-99-0 573653-00-6 573653-01-7
573653-02-8 573653-03-9

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aldosterone antagonist-NSAID combination therapy for cardiovascular disorders)

RN 95716-76-0 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, 1-methylethyl ester, (7 α ,11 α ,17 α)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

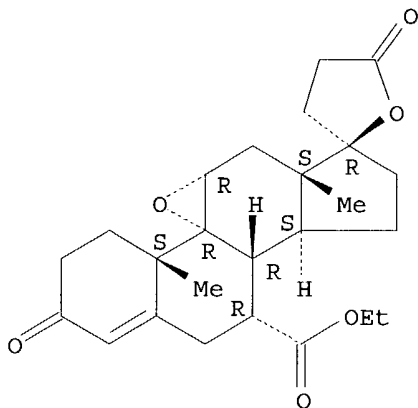


10/608,101

RN 95716-78-2 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, ethyl ester, (7 α ,11 α ,17 α)- (9CI) (CA
INDEX NAME)

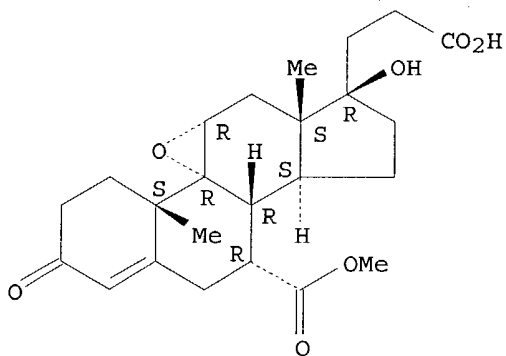
Absolute stereochemistry. Rotation (+).



RN 95716-98-6 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-methyl
ester, monopotassium salt, (7 α ,11 α ,17 α)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



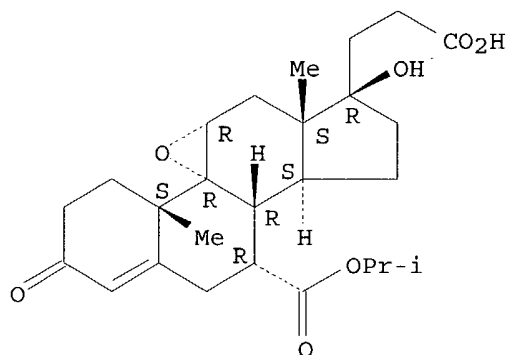
● K

RN 95716-99-7 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
7-(1-methylethyl) ester, monopotassium salt, (7 α ,11 α ,17 α)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

10/608,101

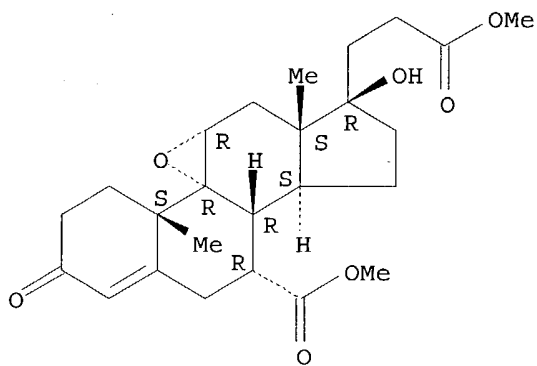


● K

RN 95717-02-5 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, dimethyl ester, (7 α ,11 α ,17 α)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

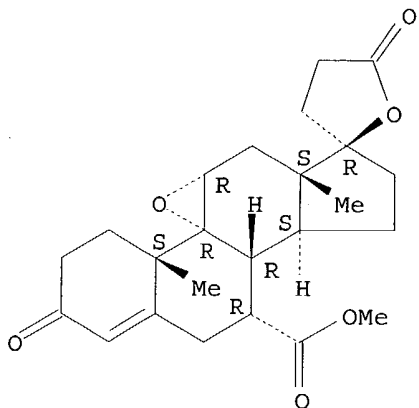


RN 107724-20-9 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, methyl ester, (7 α ,11 α ,17 α)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

10/608,101



RN 573652-78-5 CAPLUS

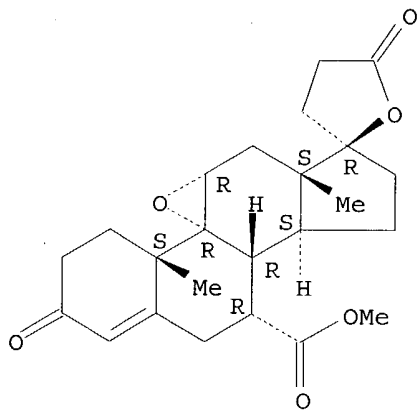
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)-, mixt. with
 N-(4-hydroxyphenyl)acetamide (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9

CMF C24 H30 O6

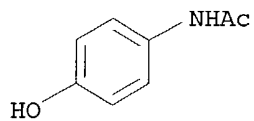
Absolute stereochemistry.



CM 2

CRN 103-90-2

CMF C8 H9 N O2



10/608,101

RN 573652-79-6 CAPLUS

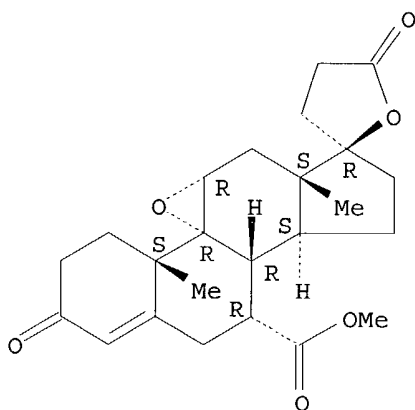
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, mixt. with
2-(4-chlorophenyl)-α-methyl-5-benzoxazoleacetic acid (9CI) (CA
INDEX NAME)

CM 1

CRN 107724-20-9

CMF C24 H30 O6

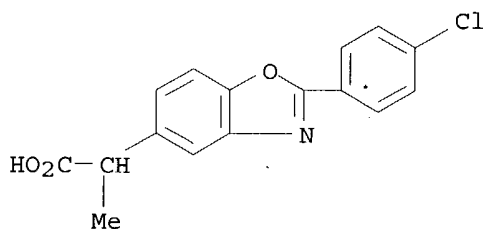
Absolute stereochemistry.



CM 2

CRN 51234-28-7

CMF C16 H12 Cl N O3



RN 573652-80-9 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, mixt. with
6-chloro-α-methyl-9H-carbazole-2-acetic acid (9CI) (CA INDEX NAME)

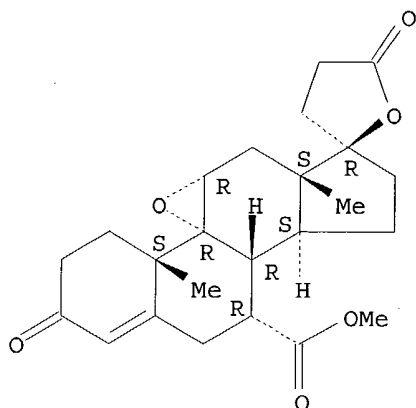
CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.

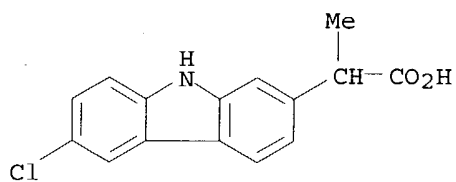
10/608,101



CM 2

CRN 53716-49-7

CMF C15 H12 Cl N O2



RN 573652-81-0 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)-, mixt. with
2-[(2,6-dichlorophenyl)amino]benzeneacetic acid (9CI) (CA INDEX NAME)

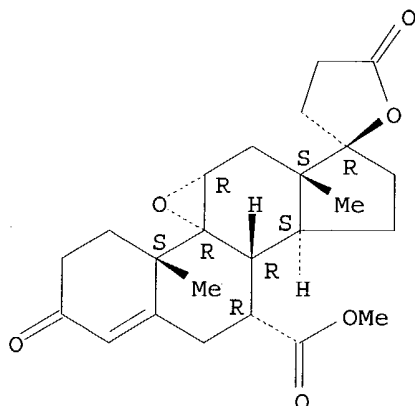
CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.

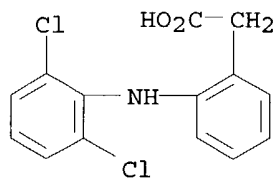
10/608,101



CM 2

CRN 15307-86-5

CMF C14 H11 Cl2 N O2



RN 573652-82-1 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)-, mixt. with
2',4'-difluoro-4-hydroxy[1,1'-biphenyl]-3-carboxylic acid (9CI) (CA INDEX
NAME)

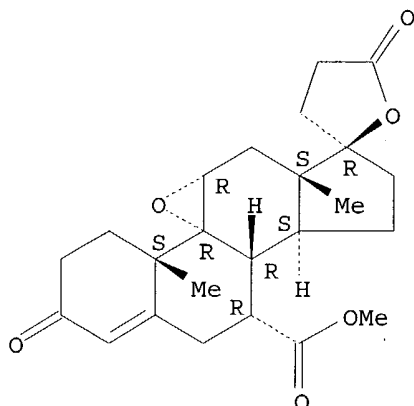
CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.

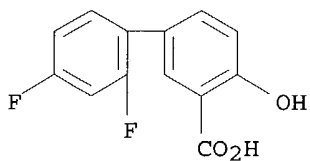
10/608,101



CM 2

CRN 22494-42-4

CMF C13 H8 F2 O3



RN 573652-83-2 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)-, mixt. with
1,8-diethyl-1,3,4,9-tetrahydropyrano[3,4-b]indole-1-acetic acid (9CI) (CA
INDEX NAME)

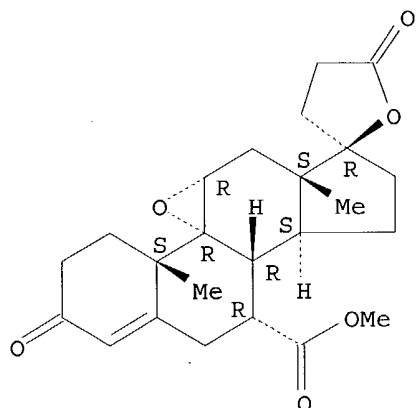
CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.

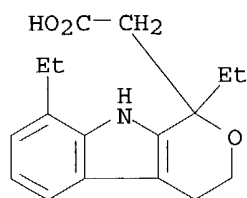
10/608,101



CM 2

CRN 41340-25-4

CMF C17 H21 N O3



RN 573652-84-3 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)-, mixt. with
 α -methyl-3-phenoxybenzeneacetic acid (9CI) (CA INDEX NAME)

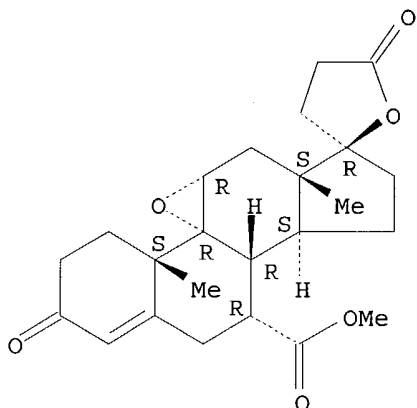
CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.

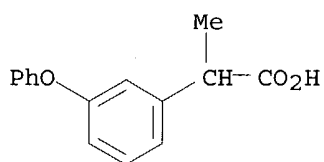
10/608,101



CM 2

CRN 29679-58-1

CMF C15 H14 O3



RN 573652-85-4 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, mixt. with
2-fluoro-α-methyl[1,1'-biphenyl]-4-acetic acid (9CI) (CA INDEX
NAME)

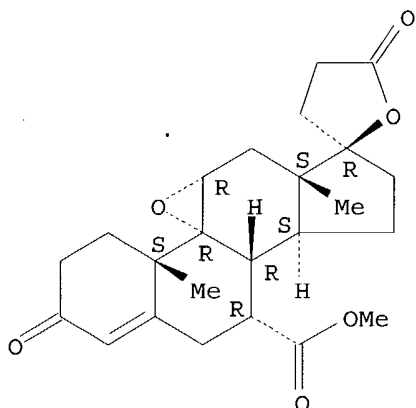
CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.

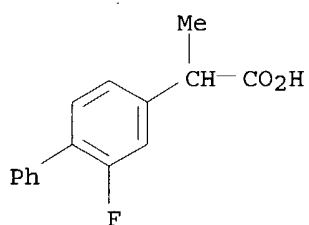
10/608,101



CM 2

CRN 5104-49-4

CMF C15 H13 F O2



RN 573652-86-5 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)-, mixt. with
 α -methyl-4-(2-methylpropyl)benzeneacetic acid (9CI) (CA INDEX NAME)

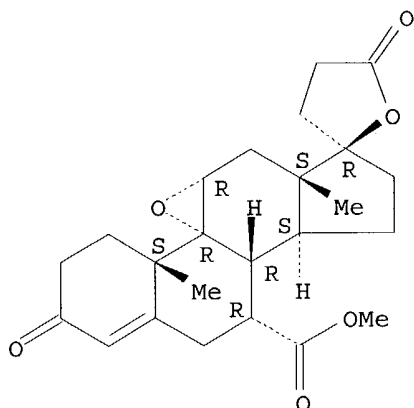
CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.

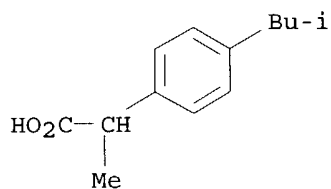
10/608,101



CM 2

CRN 15687-27-1

CMF C13 H18 O2



RN 573652-87-6 / CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)-, mixt. with
1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indole-3-acetic acid (9CI) (CA
INDEX NAME)

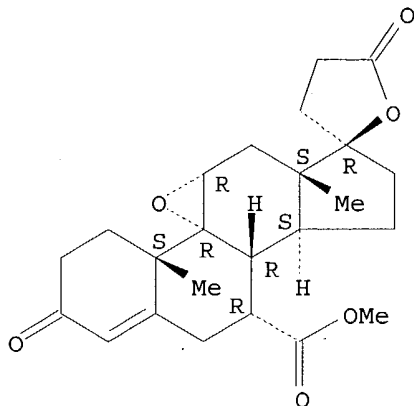
CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.

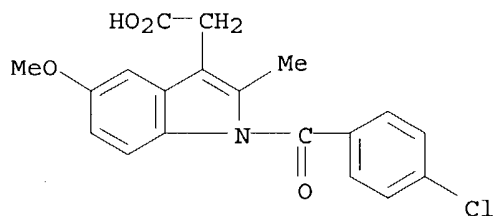
10/608,101



CM 2

CRN 53-86-1

CMF C19 H16 Cl N O4



RN 573652-88-7 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, mixt. with
3-benzoyl-α-methylbenzeneacetic acid (9CI) (CA INDEX NAME)

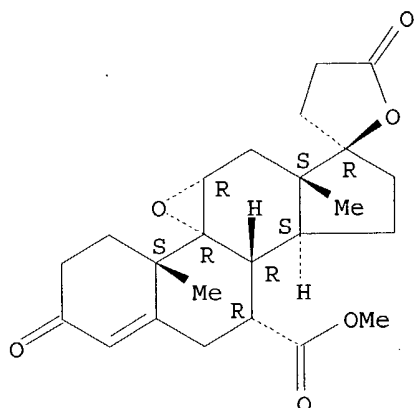
CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.

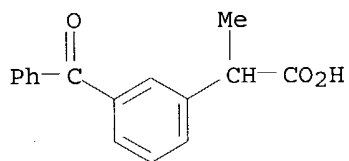
10/608,101



CM 2

CRN 22071-15-4

CMF C16 H14 O3



RN 573652-89-8 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, mixt. with
5-benzoyl-2,3-dihydro-1H-pyrrolizine-1-carboxylic acid (9CI) (CA INDEX
NAME)

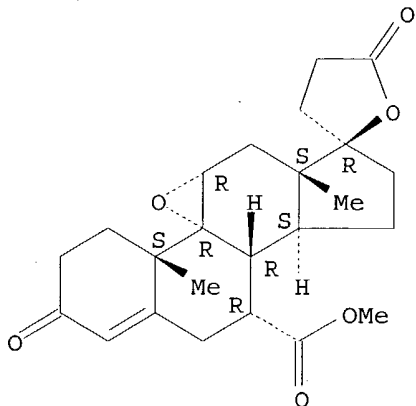
CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.

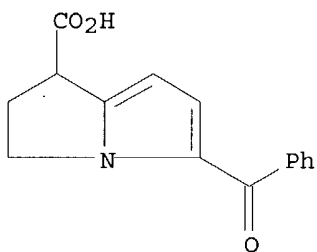
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CM 2

CRN 74103-06-3

CMF C15 H13 N O3



RN 573652-90-1 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, mixt. with
2-[(2,6-dichloro-3-methylphenyl)amino]benzoic acid (9CI) (CA INDEX NAME)

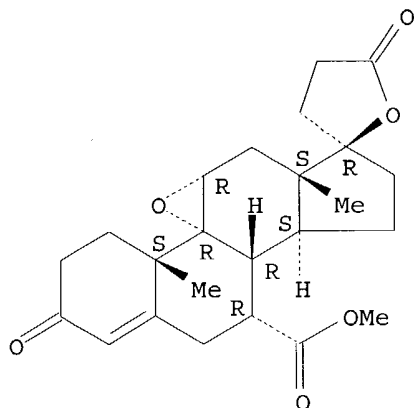
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CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.

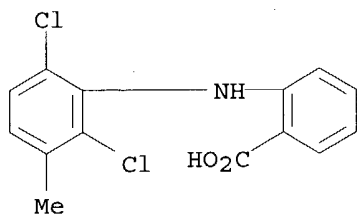
10/608,101



CM 2

CRN 644-62-2

CMF C14 H11 Cl2 N O2



RN 573652-91-2 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, mixt. with
2-[(2,3-dimethylphenyl)amino]benzoic acid (9CI) (CA INDEX NAME)

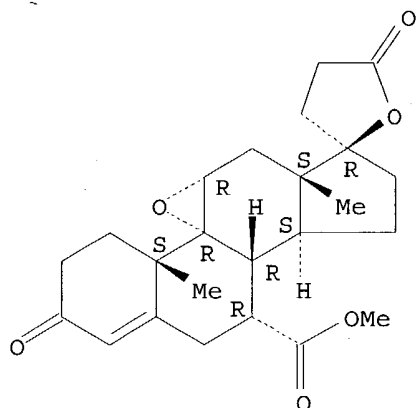
CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.

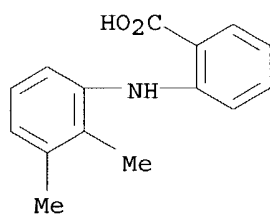
10/608,101



CM 2

CRN 61-68-7

CMF C15 H15 N O2



RN 573652-92-3 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, mixt. with
4-(6-methoxy-2-naphthalenyl)-2-butanone (9CI) (CA INDEX NAME)

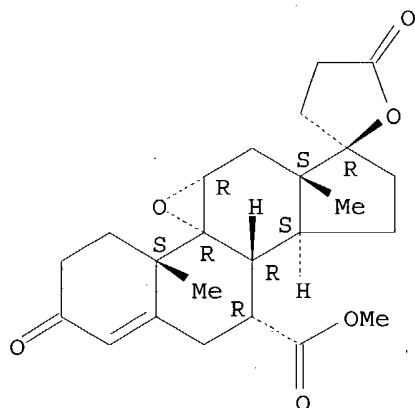
CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.

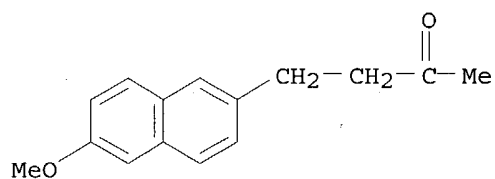
10/608,101



CM 2

CRN 42924-53-8

CMF C15 H16 O2



RN 573652-93-4 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
gamma-lactone, methyl ester, (7alpha,11alpha,17alpha)-, mixt. with
(alphaS)-6-methoxy-alpha-methyl-2-naphthaleneacetic acid (9CI) (CA
INDEX NAME)

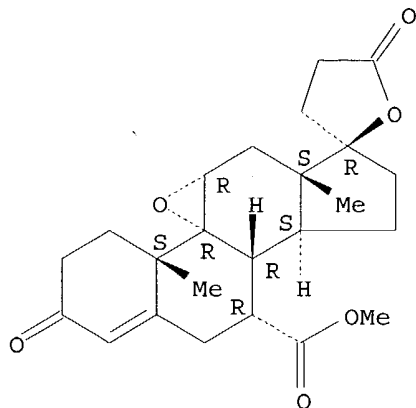
CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.

10/608,101

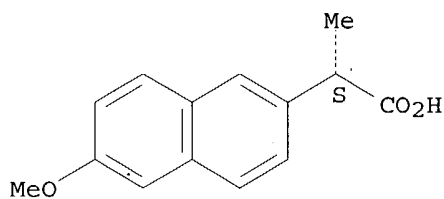


CM 2

CRN 22204-53-1

CMF C14 H14 O3

Absolute stereochemistry. Rotation (+).



RN 573652-94-5 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, mixt. with
4,5-diphenyl-2-oxazolepropanoic acid (9CI) (CA INDEX NAME)

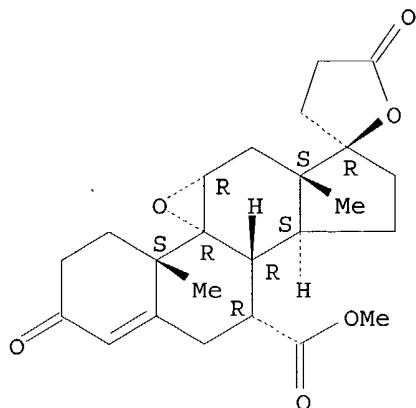
CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.

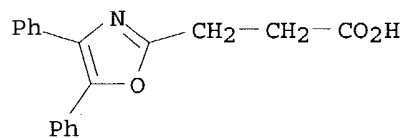
10/608,101



CM 2

CRN 21256-18-8

CMF C18 H15 N O3



RN 573652-95-6 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)-, mixt. with
4-butyl-1-(4-hydroxyphenyl)-2-phenyl-3,5-pyrazolidinedione (9CI) (CA
INDEX NAME)

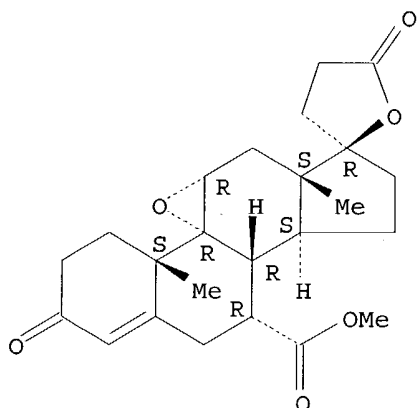
CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.

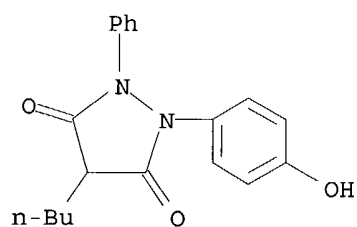
10/608,101



CM 2

CRN 129-20-4

CMF C19 H20 N2 O3



RN 573652-96-7 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, mixt. with
4-butyl-1,2-diphenyl-3,5-pyrazolidinedione (9CI) (CA INDEX NAME)

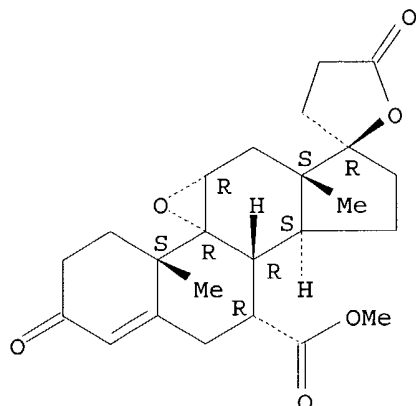
CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.

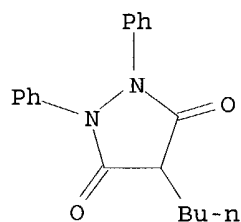
10/608,101



CM 2

CRN 50-33-9

CMF C19 H20 N2 O2



RN 573652-97-8 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, mixt. with
4-hydroxy-2-methyl-N-2-pyridinyl-2H-1,2-benzothiazine-3-carboxamide
1,1-dioxide (9CI) (CA INDEX NAME)

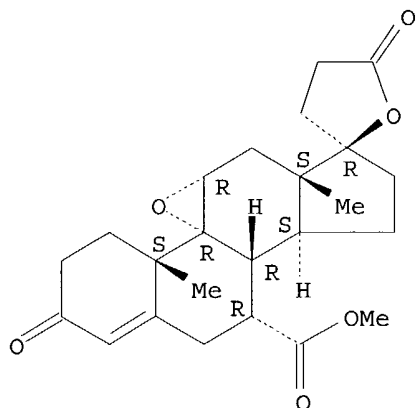
CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.

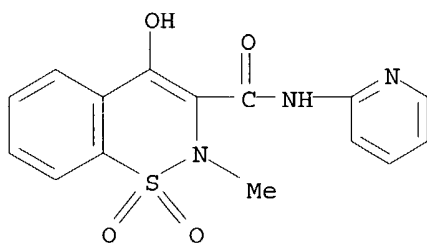
10/608,101



CM 2

CRN 36322-90-4

CMF C15 H13 N3 O4 S



RN 573652-98-9 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, mixt. with
(1Z)-5-fluoro-2-methyl-1-[[4-(methylsulfinyl)phenyl]methylene]-1H-indene-3-
acetic acid (9CI) (CA INDEX NAME)

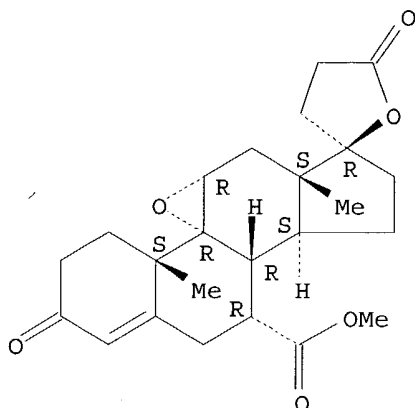
CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.

10/608,101

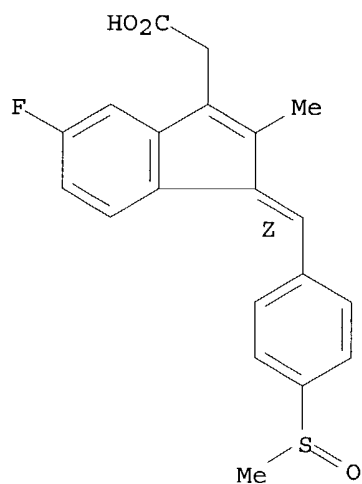


CM 2

CRN 38194-50-2

CMF C20 H17 F O3 S

Double bond geometry as shown.



RN 573652-99-0 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
gamma-lactone, methyl ester, (7alpha,11alpha,17alpha)-, mixt. with
alpha-methyl-4-(2-thienylcarbonyl)benzeneacetic acid (9CI) (CA INDEX
NAME)

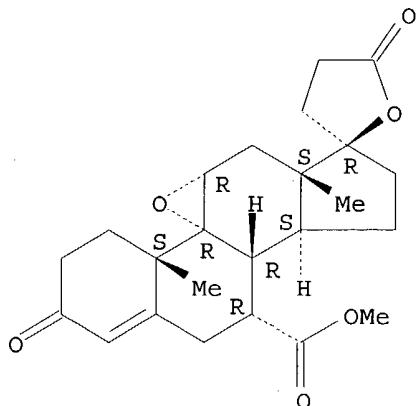
CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.

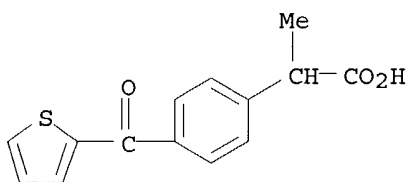
10/608,101



CM 2

CRN 40828-46-4

CMF C14 H12 O3 S



RN 573653-00-6 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)-, mixt. with
(3Z)-5-chloro-2,3-dihydro-3-(hydroxy-2-thienylmethylene)-2-oxo-1H-indole-1-
carboxamide (9CI) (CA INDEX NAME)

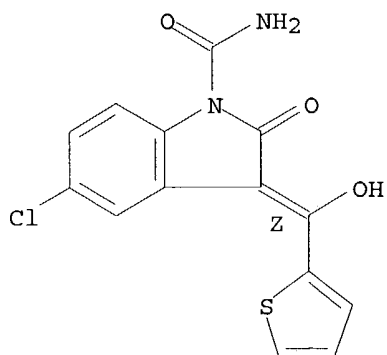
CM 1

CRN 120210-48-2

CMF C14 H9 Cl N2 O3 S

Double bond geometry as shown.

10/608,101

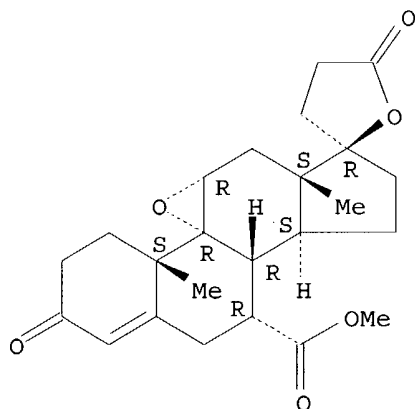


CM 2

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.



RN 573653-01-7 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)-, mixt. with
1-methyl-5-(4-methylbenzoyl)-1H-pyrrole-2-acetic acid (9CI) (CA INDEX
NAME)

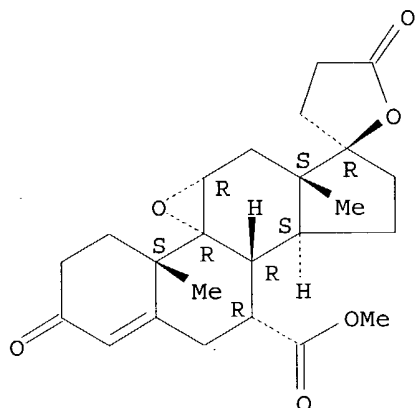
CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.

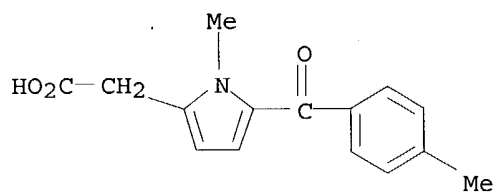
10/608,101



CM 2

CRN 26171-23-3

CMF C15 H15 N O3



RN 573653-02-8 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)-, mixt. with
5-(4-chlorobenzoyl)-1,4-dimethyl-1H-pyrrole-2-acetic acid (9CI) (CA INDEX
NAME)

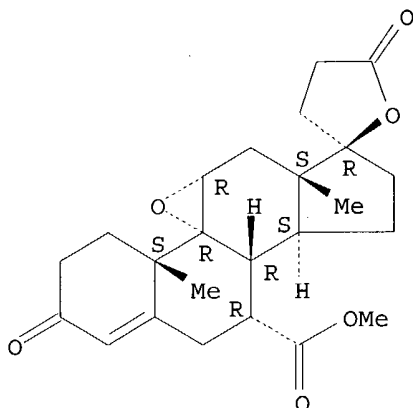
CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.

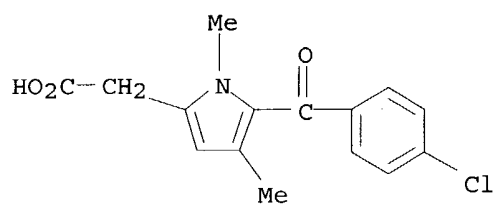
10/608,101



CM 2

CRN 33369-31-2

CMF C15 H14 Cl N O3



RN 573653-03-9 CAPLUS

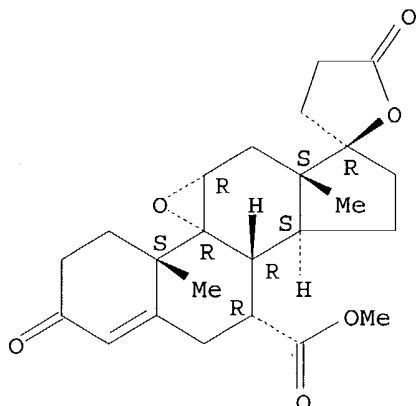
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)-, mixt. with
2-(acetyloxy)benzoic acid (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9

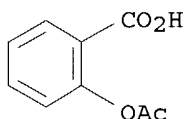
CMF C24 H30 O6

Absolute stereochemistry.



CM 2

CRN 50-78-2
CMF C9 H8 O4



AB Combinations of aldosterone blockers (e.g. eplerenone) and NSAIDs (e.g. acetaminophen) useful in the treatment of cardiovascular disorders and inflammation-related disorders are disclosed.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 12 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:610248 CAPLUS

DOCUMENT NUMBER: 139:169328

TITLE: Aldosterone receptor antagonist and alpha-adrenergic modulating agent combination therapy for prevention or treatment of pathogenic conditions

INVENTOR(S): McMahon, Ellen G.; Rudolph, Amy E.

PATENT ASSIGNEE(S): Pharmacia Corporation, USA

SOURCE: PCT Int. Appl., 75 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003063846	A2	20030807	WO 2003-US2723	20030130
WO 2003063846	A3	20031204		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,

10/608,101

PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD,
RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
ML, MR, NE, SN, TD, TG

US 2003199483 A1 20031023 US 2003-354653 20030130
PRIORITY APPLN. INFO.: US 2002-353801P P 20020130

IT 95716-76-0 95716-78-2 95716-98-6

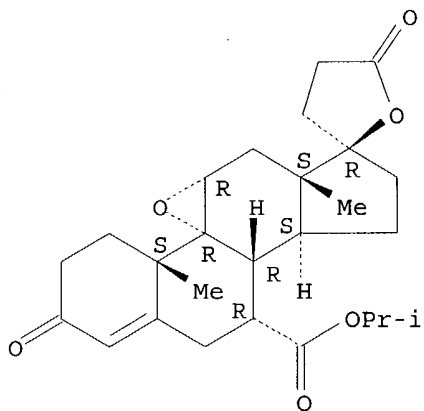
95716-99-7 95717-02-5 107724-20-9, Eplerenone

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aldosterone receptor antagonist and α -adrenergic modulators
combination therapy for prevention or treatment of pathogenic
conditions)

RN 95716-76-0 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, 1-methylethyl ester, (7 α ,11 α ,17 α)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 95716-78-2 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, ethyl ester, (7 α ,11 α ,17 α)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry. Rotation (+).

Chemical structure 1: A complex steroid derivative. It features a steroid nucleus with a ketone at C3, a double bond at C5, and a side chain at C17 containing a ketone, a methyl group, and a cyclopentane ring with a ketone. Stereochemistry is indicated with wedges and dashes.

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-methyl
 ester, monopotassium salt, (7 α ,11 α ,17 α)- (9CI) (CA
 INDEX NAME)

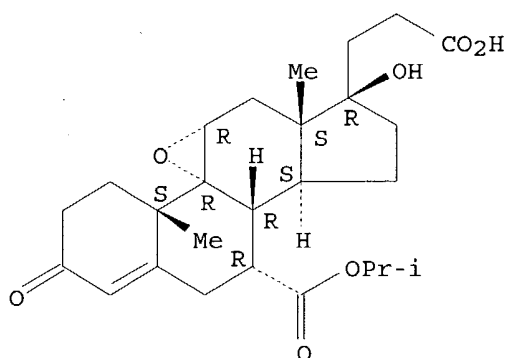
The chemical structure shows a steroid nucleus with the following features:

- A-ring:** A cyclohexenone system with a ketone at C6 and a double bond between C5 and C6.
- B-ring:** Fused to the A-ring, with a methyl group at C10 (R) and a hydrogen at C13 (H).
- C-ring:** Fused to the B-ring, with a methyl group at C13 (Me) and a hydrogen at C14 (H).
- D-ring:** Fused to the C-ring, with a methyl group at C13 (Me), a hydrogen at C14 (H), and a side chain at C17.
- Side chain at C17:** -CH₂-CH(OH)-CH₂-CO₂H.
- Other substituents:** A methyl ketone at C3 (-C(=O)OMe) and a methyl group at C10 (R).

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
7-(1-methylethyl) ester, monopotassium salt, (7 α ,11 α ,17 α
) - (9CI) (CA INDEX NAME)

Page 57

10/608,101

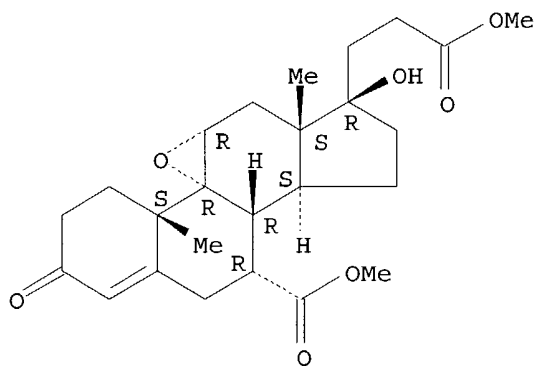


● K

RN 95717-02-5 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, dimethyl ester, (7 α ,11 α ,17 α)- (9CI) (CA INDEX NAME)

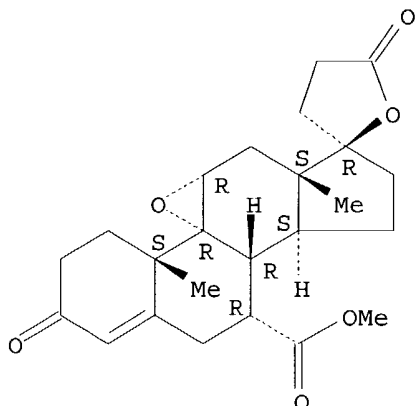
Absolute stereochemistry.



RN 107724-20-9 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, methyl ester, (7 α ,11 α ,17 α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB A combination therapy comprising a therapeutically-effective amount of an aldosterone receptor antagonist and a amount of an α -adrenergic modulating agent is described for treatment of circulatory disorders, including cardiovascular disorders such as hypertension, congestive heart failure, cirrhosis and ascites. Preferred α -adrenergic modulating agents are those compds. having high potency and bioavailability. Preferred aldosterone receptor antagonists are 20-spiroxane steroidal compds. characterized by the presence of a 9,11-substituted epoxy moiety. A preferred combination therapy includes an α 1-adrenergic antagonist or an α 2-adrenergic agonist and the aldosterone receptor antagonist epoxymexrenone. Thus, a solution contains 0.5% dapiprazole and eplerenone.

L8 ANSWER 13 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2003:1007852 CAPLUS
 DOCUMENT NUMBER: 140:47560
 TITLE: Pharmaceutical compositions and dosage forms for administration of hydrophobic drugs
 INVENTOR(S): Chen, Feng-Jing; Patel, Mahesh V.; Fikstad, David T.; Zhang, Huiping; Gilyar, Chandrashekar
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 18 pp., Cont.-in-part of U.S. Pat. Appl. 2002 32,171.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 12
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003236236	A1	20031225	US 2003-444935	20030522
US 6267985	B1	20010731	US 1999-345615	19990630
US 6309663	B1	20011030	US 1999-375636	19990817
US 2001024658	A1	20010927	US 2000-751968	20001229
US 6458383	B2	20021001		
US 2002032171	A1	20020314	US 2001-877541	20010608
US 6761903	B2	20040713		
PRIORITY APPLN. INFO.:			US 1999-345615	A2 19990630
			US 1999-375636	A2 19990817
			US 2000-716029	A2 20001117
			US 2000-751968	A2 20001229
			US 2001-877541	A2 20010608

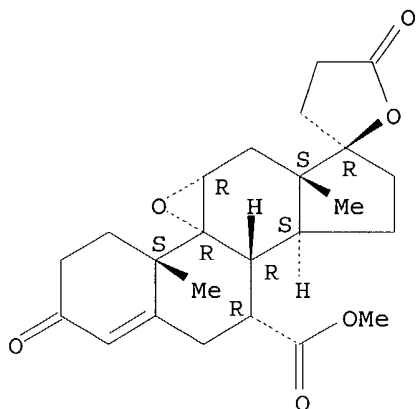
IT 107724-20-9, Eplerenone

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (pharmaceutical compns. containing hydrophobic drugs and solubilizers for
 enhancement of bioavailability)

RN 107724-20-9 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)- (9CI) (CA
 INDEX NAME)

Absolute stereochemistry.



AB Pharmaceutical compns. and dosage forms for administration of hydrophobic drugs, particularly **steroids**, are provided. The pharmaceutical compns. include a therapeutically effective amount of a hydrophobic drug, preferably a steroid; a solubilizer, preferably a vitamin E substance; and a surfactant. The synergistic effect between the hydrophobic drug and the vitamin E substance results in a pharmaceutical formulation with improved dispersion of both the active agent and the solubilizer. As a result of the improved dispersion, the pharmaceutical composition has improved bioavailability upon administration. Methods of improving the bioavailability of hydrophobic drugs are also provided. For example, a dispersion was formulated containing dl- α -tocopherol 313, Cremophor EL 256, dehydrated alc. 70, and progesterone 60 mg.

L8 ANSWER 14 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:678514 CAPLUS

DOCUMENT NUMBER: 139:191440

TITLE: Methods of treating or preventing a cardiovascular
 condition using a cyclooxygenase-1 inhibitor

INVENTOR(S): Krul, Elaine S.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 32 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003162824	A1	20030828	US 2002-292255	20021112
PRIORITY APPLN. INFO.:			US 2001-331346P	P 20011112

OTHER SOURCE(S): MARPAT 139:191440

IT 107724-20-9, Eplerenone

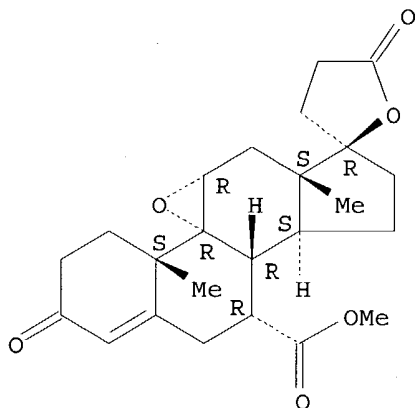
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(aldosterone receptor antagonist; cyclooxygenase-1 inhibitor for treating or preventing cardiovascular conditions)

RN 107724-20-9 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, methyl ester, (7 α ,11 α ,17 α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB Methods for treating or preventing one or more cardiovascular conditions in a subject comprises treating the subject with a therapeutically effective amount of a selective cyclooxygenase-1 inhibitor or a pharmaceutically-acceptable salt, tautomer or prodrug thereof alone or in combination with either a drug used in the treatment or prevention of a cardiovascular condition or a non-drug therapy used in the treatment of a cardiovascular condition. Cyclooxygenase-1 inhibitor, 5-(4-Chlorophenyl)-1-(4-methoxyphenyl)-3-(trifluoromethyl)pyrazole (I), was prepared from 4'-chloroacetophenone and (4-methoxyphenyl)hydrazine hydrochloride. I inhibited development of atherosclerosis in cholesterol-fed apoE knockout mice.

L8 ANSWER 15 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:396452 CAPLUS

DOCUMENT NUMBER: 138:363210

TITLE: Methods for the treatment or prophylaxis of aldosterone-mediated pathogenic effects in a subject using an epoxy-steroidal aldosterone antagonist

INVENTOR(S): Williams, Gordon H.; Funder, John W.; Garthwaite, Susan M.; Roniker, Barbara; Fedde, Kenton N.; Rocha, Ricardo

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 242 pp., Cont.-in-part of U.S. Ser. No. 713,348.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003096798	A1	20030522	US 2001-17288	20011213
US 2003125312	A1	20030703	US 2001-915784	20010726
US 6716829	B2	20040406		
US 2003191100	A1	20031009	US 2002-243876	20020913
US 2003203884	A1	20031030	US 2003-354823	20030130
US 2004067916	A1	20040408	US 2003-648863	20030826
US 2004102424	A1	20040527	US 2003-682527	20031009
PRIORITY APPLN. INFO.:			US 1999-164390P	P 19991109
			US 2000-211064P	P 20000613
			US 2000-211250P	P 20000613
			US 2000-211253P	P 20000613
			US 2000-211264P	P 20000613
			US 2000-211311P	P 20000613
			US 2000-211340P	P 20000613
			US 2000-211451P	P 20000613
			US 2000-211459P	P 20000613
			US 2000-221358P	P 20000727
			US 2000-221364P	P 20000727
			US 2000-233056P	P 20000914
			US 2000-709253	A2 20001108
			US 2000-713348	A2 20001114
			US 2000-712543	A1 20001114
			US 2001-261352P	P 20010112
			US 2001-261497P	P 20010112
			US 2001-17288	B1 20011213

IT 107724-20-9DP, Eplerenone, derivs.

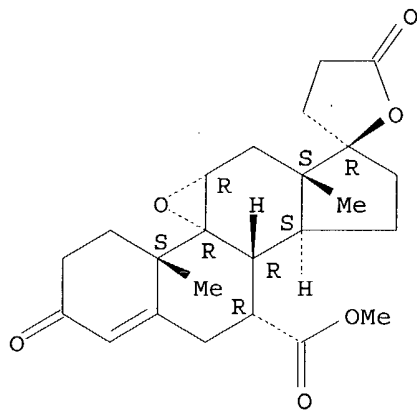
RL: PAC (Pharmacological activity); PEP (Physical, engineering or chemical process); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(antihypertensive, renal, and metabolic effects of eplerenone and enalapril in patients with type 2 diabetes, albuminuria, and hypertension)

RN 107724-20-9 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, methyl ester, (7 α ,11 α ,17 α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



10/608,101

IT 107724-20-9P, Eplerenone

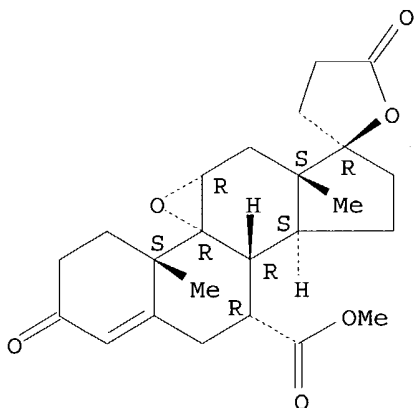
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(use of epoxy-steroidal aldosterone antagonist for treatment or prophylaxis of aldosterone-mediated pathogenic effects)

RN 107724-20-9 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, methyl ester, (7 α ,11 α ,17 α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 95716-76-0P 95716-78-2P 95716-98-6P

95716-99-7P 95717-02-5P

RL: PAC (Pharmacological activity); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

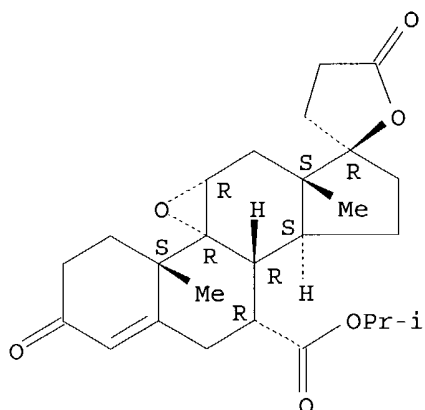
(use of epoxy-steroidal aldosterone antagonist for treatment or prophylaxis of aldosterone-mediated pathogenic effects)

RN 95716-76-0 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, 1-methylethyl ester, (7 α ,11 α ,17 α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

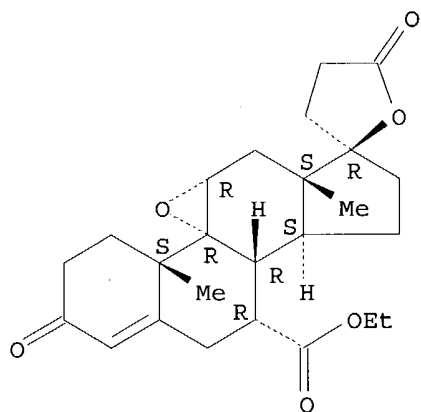
10/608,101



RN 95716-78-2 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, ethyl ester, (7 α ,11 α ,17 α)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry. Rotation (+).

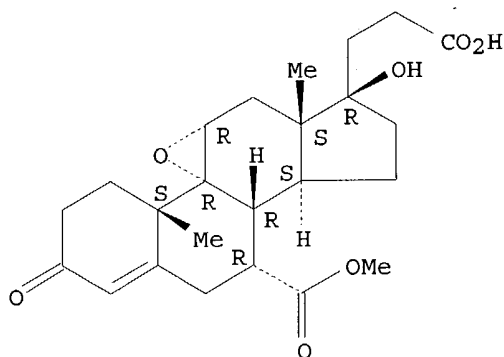


RN 95716-98-6 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-methyl
ester, monopotassium salt, (7 α ,11 α ,17 α)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

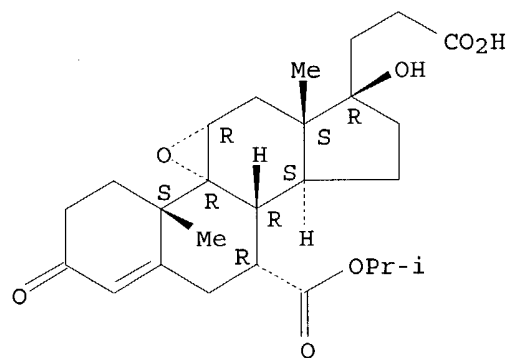
10/608,101



● K

RN 95716-99-7 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
7-(1-methylethyl) ester, monopotassium salt, (7 α ,11 α ,17 α) - (9CI) (CA INDEX NAME)

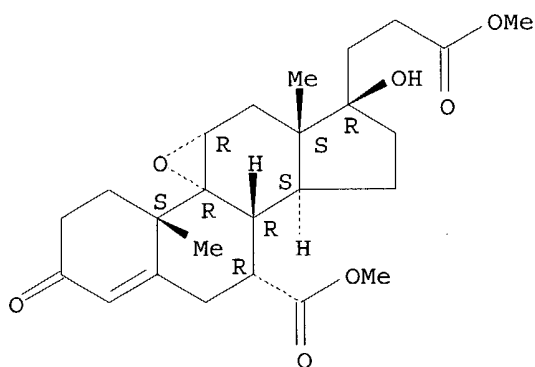
Absolute stereochemistry.



● K

RN 95717-02-5 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, dimethyl
ester, (7 α ,11 α ,17 α) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB The present invention provides methods for the treatment or prophylaxis of one or more aldosterone-mediated pathogenic effects in a subject suffering from or susceptible to the pathogenic effect or effects wherein the subject has one or more conditions selected from the group consisting of a sub-normal endogenous aldosterone level, salt sensitivity and an elevated dietary sodium intake. The methods comprise administering to the subject a therapeutically-effective amount of one or more epoxy-steroidal compds. that are aldosterone antagonists.

L8 ANSWER 16 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:930970 CAPLUS

DOCUMENT NUMBER: 140:743

TITLE: Epoxy-steroidal aldosterone antagonist and calcium channel blocker combination therapy for treatment of cardiovascular disorders

INVENTOR(S): Schuh, Joseph R.

PATENT ASSIGNEE(S): G.D. Searle and Co., USA

SOURCE: U.S. Pat. Appl. Publ., 87 pp., Cont.-in-part of U.S. Ser. No. 126134, abandoned.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003220312	A1	20031127	US 2002-324330	20021219
US 2002132001	A1	20020919	US 2001-854264	20010511
US 2002042405	A1	20020411	US 2001-917425	20010727
US 2003055027	A1	20030320	US 2002-126134	20020419
PRIORITY APPLN. INFO.:			US 2000-203637P	P 20000511
			US 2000-221359P	P 20000727
			US 2001-854264	A1 20010511
			US 2001-917425	B1 20010727
			US 2002-126134	B2 20020419

IT 107724-20-9P, Eplerenone

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); PUR (Purification or recovery); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

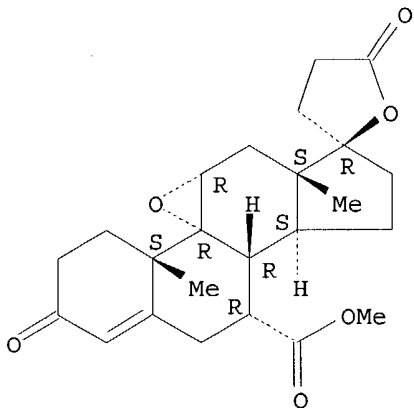
(epoxy-steroidal aldosterone antagonist; epoxy-steroidal aldosterone antagonist and calcium channel blocker combination therapy for treatment of cardiovascular disorders)

10/608,101

RN 107724-20-9 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



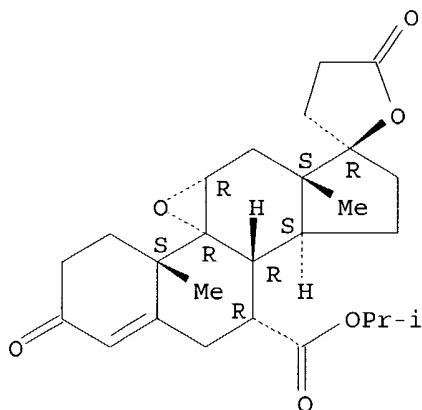
IT **95716-76-0**, Pregn-4-ene-7,21-dicarboxylic acid, **9,11-epoxy**-17-hydroxy-3-oxo-,γ-lactone,
1-methylethyl ester, (7α,11α,17α)- **95716-78-2**,
Pregn-4-ene-7,21-dicarboxylic acid, **9,11-epoxy**
-17-hydroxy-3-oxo-,γ-lactone, ethyl ester,
(7α,11α,17α)- **95716-98-6**, Pregn-4-ene-7,21-
dicarboxylic acid,**9,11-epoxy**
-17-hydroxy-3-oxo-,7-methyl ester monopotassium salt,
(7α,11α,17α)- **95716-99-7**, Pregn-4-ene-7,21-
dicarboxylic acid, **9,11-epoxy**
-17-hydroxy-3-oxo-,7-(1-methylethyl) ester monopotassium
salt, (7α,11α,17α)- **95717-02-5**,
Pregn-4-ene-7,21-dicarboxylic acid **9,11-epoxy**
-17-hydroxy-3-oxodimethyl ester, (7α,11α,17α)-
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(epoxy-steroidal aldosterone antagonist; epoxy-steroidal aldosterone
antagonist and calcium channel blocker combination therapy for
treatment of cardiovascular disorders)

RN 95716-76-0 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, 1-methylethyl ester, (7α,11α,17α)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

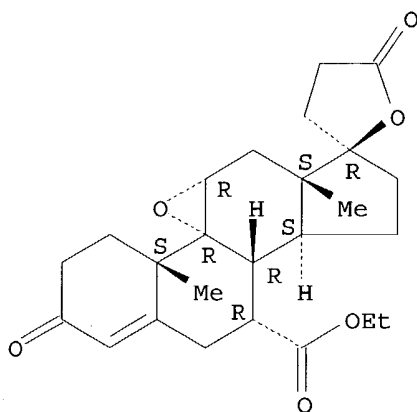
10/608,101



RN 95716-78-2 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, ethyl ester, (7 α ,11 α ,17 α)-(9CI) (CA
INDEX NAME)

Absolute stereochemistry. Rotation (+).

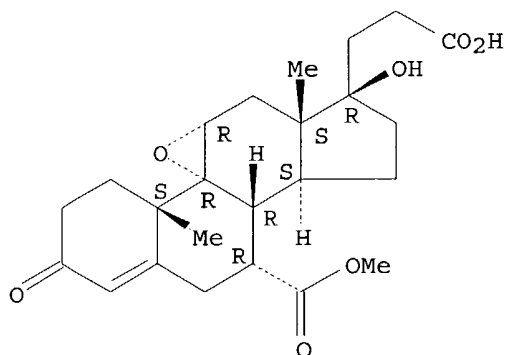


RN 95716-98-6 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-methyl
ester, monopotassium salt, (7 α ,11 α ,17 α)-(9CI) (CA
INDEX NAME)

Absolute stereochemistry.

10/608,101

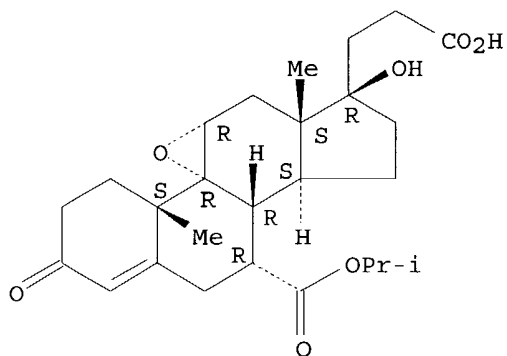


● K

RN 95716-99-7 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
7-(1-methylethyl) ester, monopotassium salt, (7 α ,11 α ,17 α) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

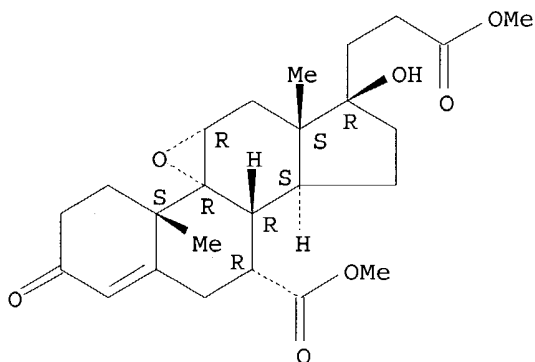


● K

RN 95717-02-5 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, dimethyl
ester, (7 α ,11 α ,17 α) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB A combination therapy comprising a therapeutically-effective amount of an epoxy-steroidal aldosterone receptor antagonist and a therapeutically-effective amount of a calcium channel blocker is described for treatment of circulatory disorders, including cardiovascular disorders such as hypertension, angina and congestive heart failure. Preferred calcium channel blockers are those compds. having high potency and bioavailability. Preferred epoxy-steroidal aldosterone receptor antagonists are 20-spiroxane steroidal compds. characterized by the presence of a $9\alpha,11\alpha$ -substituted epoxy moiety. A preferred combination therapy includes the calcium channel blocker amlodipine and the aldosterone receptor antagonist eplerenone.

L8 ANSWER 17 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:449846 CAPLUS

DOCUMENT NUMBER: 137:29820

TITLE: Cloning, characterization and use of steroid
11 α -hydroxylase and cytochrome P 450
oxidoreductase from *Aspergillus ochraceus*

INVENTOR(S): Bolton, Suzanne; Clayton, Robert; Easton, Alan; Engel,
Leslie; Messing, Dean

PATENT ASSIGNEE(S): Pharmacia Corporation, USA

SOURCE: PCT Int. Appl., 181 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

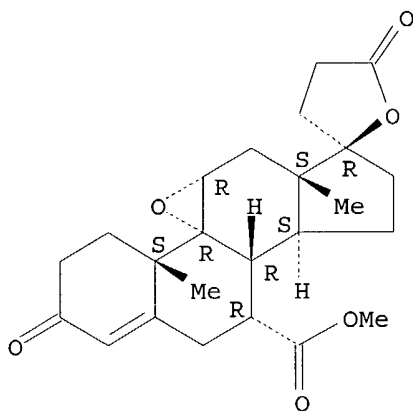
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002046386	A2	20020613	WO 2001-US51070	20011026
WO 2002046386	A3	20030807		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2002041768	A5	20020618	AU 2002-41768	20011026
EP 1352054	A2	20031015	EP 2001-988464	20011026
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,			

10/608,101

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
US 2003148420 A1 20030807 US 2001-21425 20011030
PRIORITY APPLN. INFO.: US 2000-244300P P 20001030
WO 2001-US51070 W 20011026
IT 107724-20-9P, Eplerenone
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
BIOL (Biological study); PREP (Preparation)
(cloning, characterization and use of steroid 11 α -hydroxylase and
cytochrome P 450 oxidoreductase from *Aspergillus ochraceus*)
RN 107724-20-9 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



AB The present invention relates to a novel cytochrome P 450-like enzyme (*Aspergillus ochraceus* 11 α -hydroxylase) and an oxidoreductase (*Aspergillus ochraceus* oxidoreductase) isolated from cDNA library generated from the mRNA of *Aspergillus ochraceus* spores. When the cDNA encoding the 11 α -hydroxylase was co-expressed in *Spodoptera frugiperda* (Sf-9) insect cells with the cDNA encoding human oxidoreductase as an electron donor, it successfully catalyzed the conversion of the steroid substrate 4-androstene-3,17-dione (AD) to 11- α -hydroxy-AD as determined by HPLC anal. The invention also relates to nucleic acid mols. associated with or derived from these cDNAs including complements, homologues and fragments thereof, and methods of using these nucleic acid mols., to generate, for example, polypeptides and fragments thereof. The invention also relates to the generation of antibodies that recognizes the *A. ochraceus* 11- α -hydroxylase and oxidoreductase and methods of using these antibodies to detect the presence of these native and recombinant polypeptides within unmodified and transformed host cells, resp. The invention also provides methods of expressing the *Aspergillus* 11- α -hydroxylase gene sep., or in combination with human or *Aspergillus* oxidoreductase, in heterologous host cells, to facilitate the bioconversion of steroid substances to their 11- α -hydroxy-counterparts.

L8 ANSWER 18 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:171665 CAPLUS
DOCUMENT NUMBER: 136:210586
TITLE: Use of an aldosterone receptor antagonist to improve
cognitive function

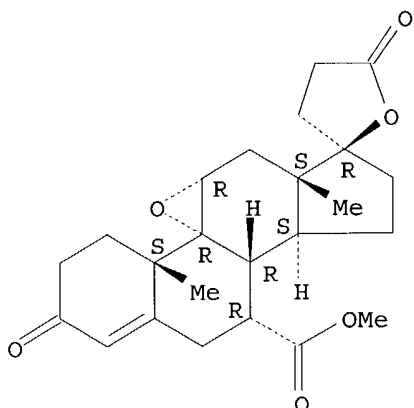
10/608,101

INVENTOR(S): Fedde, Kenton N.; Perez, Alfonso T.; Tooley, Joseph F.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 177 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002017895	A2	20020307	WO 2001-US26760	20010828
WO 2002017895	A3	20030206		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001085318	A5	20020313	AU 2001-85318	20010828
US 2002111337	A1	20020815	US 2001-941206	20010828
EP 1313485	A2	20030528	EP 2001-964471	20010828
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004507495	T2	20040311	JP 2002-522869	20010828
PRIORITY APPLN. INFO.:			US 2000-228738P	P 20000828
			WO 2001-US26760	W 20010828
IT	344450-03-9 344450-04-0 344450-09-5 344450-11-9 396068-72-7 396068-73-8 396068-74-9 396068-76-1 396068-77-2 396068-78-3 396068-79-4 396068-80-7 396068-81-8 396068-82-9 396068-83-0 396068-84-1 396068-85-2 396077-49-9 402718-58-5 402718-59-6 402718-60-9			
RL: PRP (Properties) (eplerenone crystalline solvate; use of aldosterone receptor antagonist to improve cognitive function and treat diseases and improve quality of life)				
RN	344450-03-9 CAPLUS			
CN	Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, methyl ester, (7 α ,11 α ,17 α)-, compd. with 1,1-dimethylethyl acetate (9CI) (CA INDEX NAME)			
CM	1			
CRN	107724-20-9			
CMF	C24 H30 O6			

Absolute stereochemistry.

10/608,101



CM 2

CRN 540-88-5
CMF C6 H12 O2

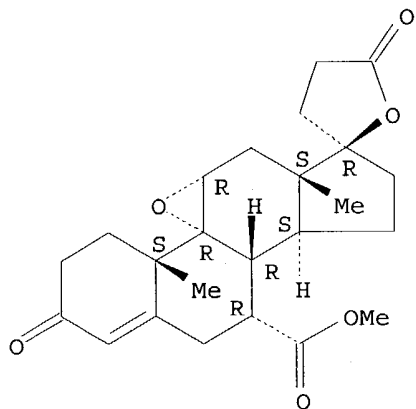
t-Bu-O-Ac

RN 344450-04-0 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with trichloromethane (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9
CMF C24 H30 O6

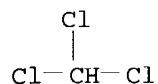
Absolute stereochemistry.



CM 2

10/608,101

CRN 67-66-3
CMF C H Cl3

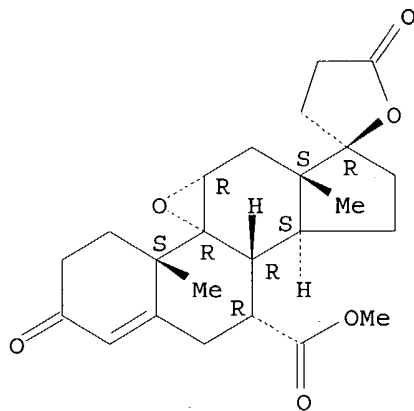


RN 344450-09-5 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)-, compd.
with 1-octanol (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9
CMF C24 H30 O6

Absolute stereochemistry.



CM 2

CRN 111-87-5
CMF C8 H18 O

HO-(CH₂)₇-Me

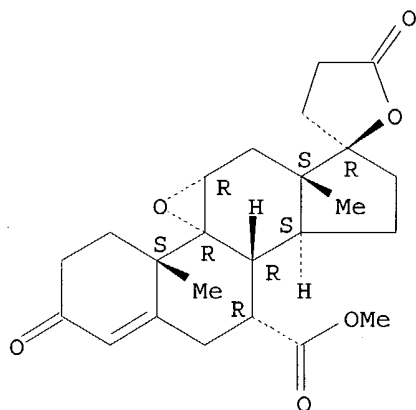
RN 344450-11-9 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)-, compd.
with 1,2-propanediol (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9
CMF C24 H30 O6

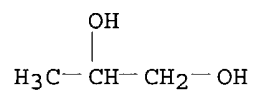
Absolute stereochemistry.

10/608,101



CM 2

CRN 57-55-6
CMF C3 H8 O2

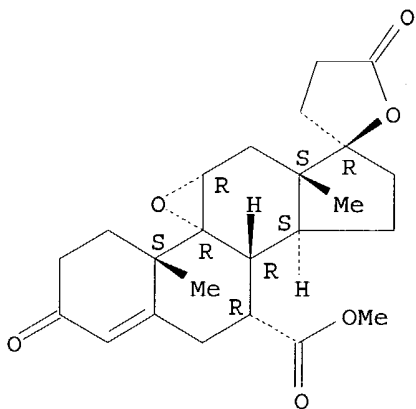


RN 396068-72-7 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
gamma-lactone, methyl ester, (7alpha,11alpha,17alpha)-, compd.
with 2-butanone (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9
CMF C24 H30 O6

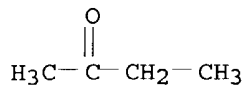
Absolute stereochemistry.



CM 2

10/608,101

CRN 78-93-3
CMF C4 H8 O

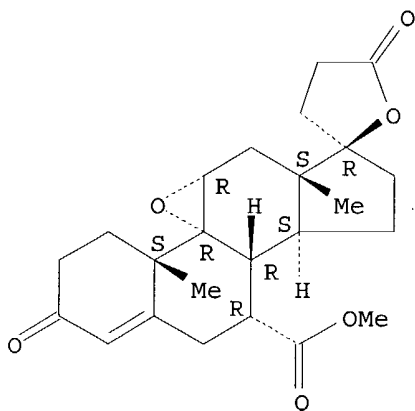


RN 396068-73-8 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)-, compd.
with 2-propanone (1:1) (9CI) (CA INDEX NAME)

CM 1

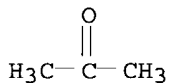
CRN 107724-20-9
CMF C24 H30 O6

Absolute stereochemistry.



CM 2

CRN 67-64-1
CMF C3 H6 O



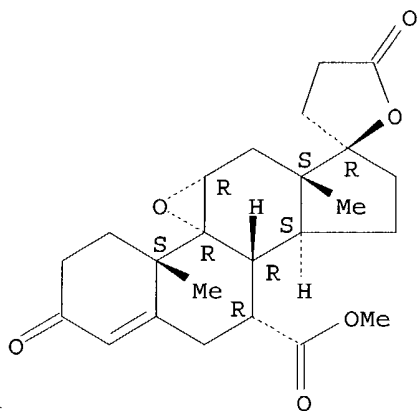
RN 396068-74-9 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)-, compd.
with methylbenzene (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9
CMF C24 H30 O6

10/608,101

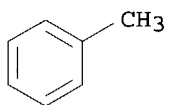
Absolute stereochemistry.



CM 2

CRN 108-88-3

CMF C7 H8



RN 396068-76-1 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)-, compd.
with 2-methylpropyl acetate (2:1) (9CI) (CA INDEX NAME)

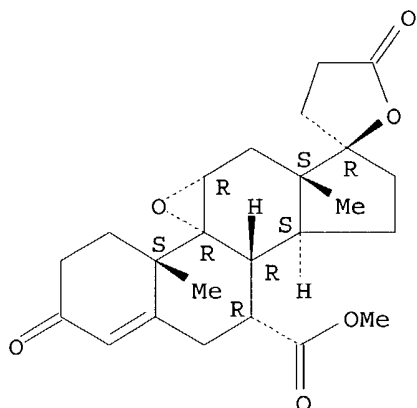
CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.

10/608,101



CM 2

CRN 110-19-0

CMF C6 H12 O2

i-Bu-O-Ac

RN 396068-77-2 CAPLUS

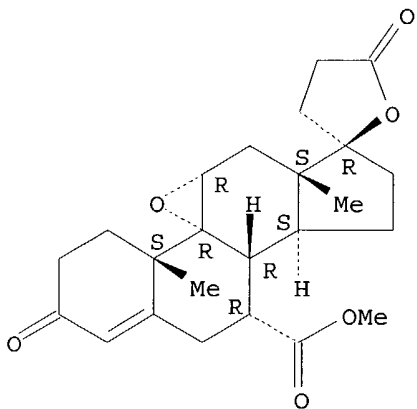
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with 2-propanol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9

CMF C24 H30 O6

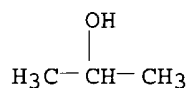
Absolute stereochemistry.



CM 2

10/608,101

CRN 67-63-0
CMF C3 H8 O

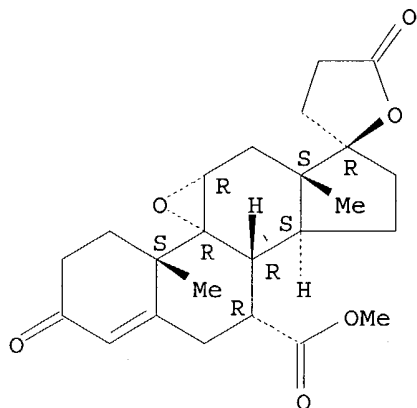


RN 396068-78-3 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with ethanol (1:1) (9CI) (CA INDEX NAME)

CM 1

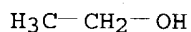
CRN 107724-20-9
CMF C24 H30 O6

Absolute stereochemistry.



CM 2

CRN 64-17-5
CMF C2 H6 O



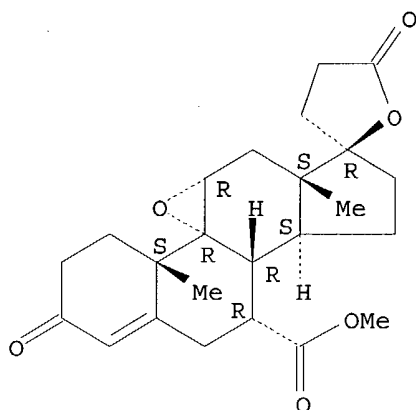
RN 396068-79-4 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with acetic acid (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9
CMF C24 H30 O6

Absolute stereochemistry.

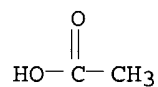
10/608,101



CM 2

CRN 64-19-7

CMF C2 H4 O2



RN 396068-80-7 CAPLUS

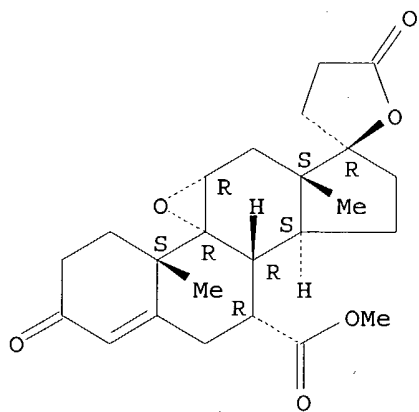
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with methyl acetate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9

CMF C24 H30 O6

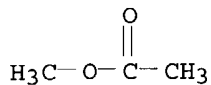
Absolute stereochemistry.



CM 2

10/608,101

CRN 79-20-9
CMF C3 H6 O2

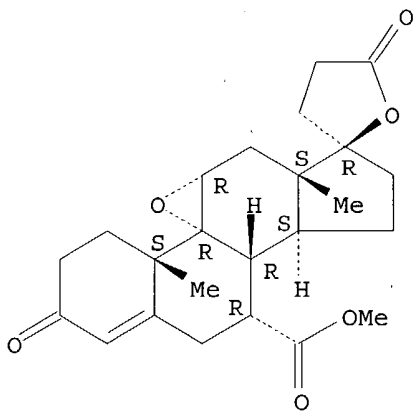


RN 396068-81-8 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with ethyl propanoate (1:1) (9CI) (CA INDEX NAME)

CM 1

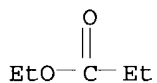
CRN 107724-20-9
CMF C24 H30 O6

Absolute stereochemistry.



CM 2

CRN 105-37-3
CMF C5 H10 O2



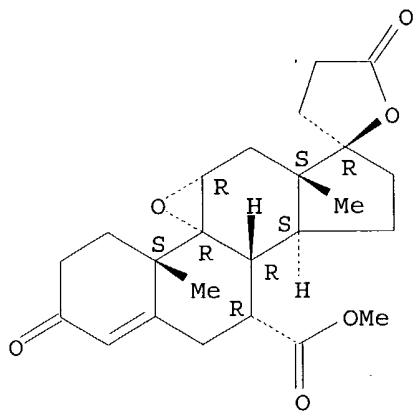
RN 396068-82-9 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with 1-butanol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9
CMF C24 H30 O6

10/608,101

Absolute stereochemistry.



CM 2

CRN 71-36-3
CMF C4 H10 O

$$\text{H}_3\text{C}-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{OH}$$

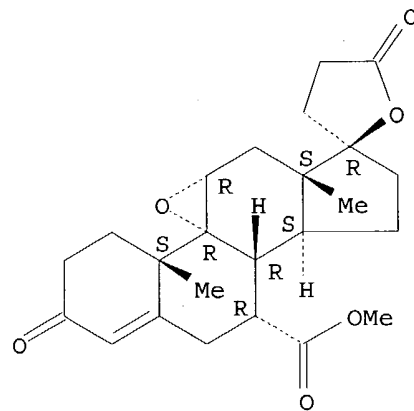
RN 396068-83-0 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ-lactone, methyl ester, (7α,11α,17α)-, compd.
 with 1-propanol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9
CMF C24 H30 O6

Absolute stereochemistry.



10/608,101

CM 2

CRN 71-23-8

CMF C3 H8 O

$\text{H}_3\text{C}-\text{CH}_2-\text{CH}_2-\text{OH}$

RN 396068-84-1 CAPLUS

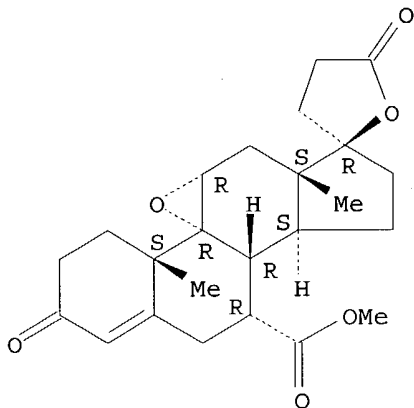
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)-, compd.
with propyl acetate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.



CM 2

CRN 109-60-4

CMF C5 H10 O2

$\text{n-Pr}-\text{O}-\text{Ac}$

RN 396068-85-2 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)-, compd.
with tetrahydrofuran (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.

CRN 109-99-9
CMF C4 H8 O



CM 1

CRN 107724-20-9
CMF C24 H30 O6

Page 84

10/608,101

CRN 123-86-4
CMF C6 H12 O2

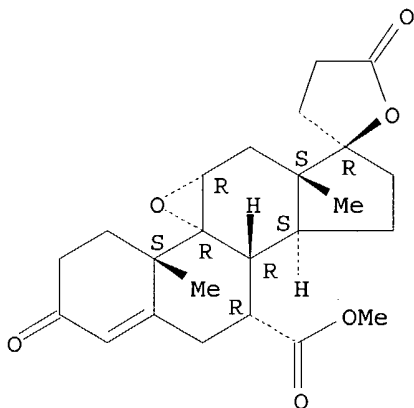
n-Bu-O-Ac

RN 402718-58-5 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with 2-pentanone (9CI) (CA INDEX NAME)

CM 1

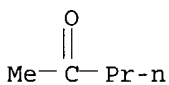
CRN 107724-20-9
CMF C24 H30 O6

Absolute stereochemistry.



CM 2

CRN 107-87-9
CMF C5 H10 O



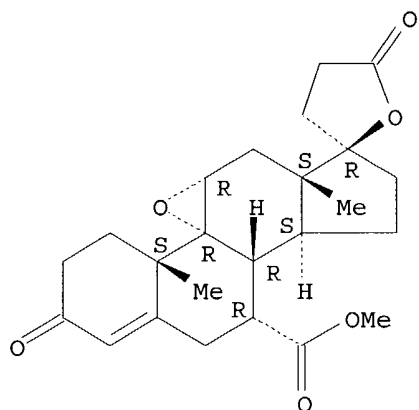
RN 402718-59-6 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with 2-methyl-1-propanol (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9
CMF C24 H30 O6

Absolute stereochemistry.

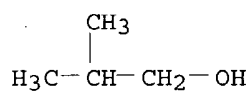
10/608,101



CM 2

CRN 78-83-1

CMF C4 H10 O



RN 402718-60-9 CAPLUS

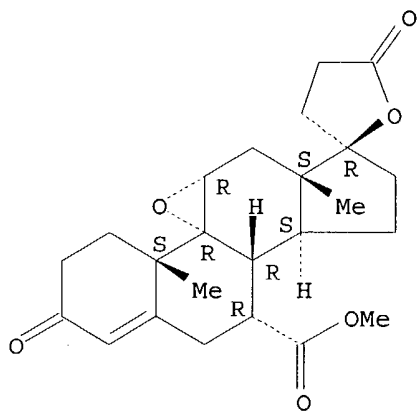
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with 2-methyl-2-propanol (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9

CMF C24 H30 O6

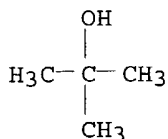
Absolute stereochemistry.



10/608,101

CM 2

CRN 75-65-0
CMF C4 H10 O



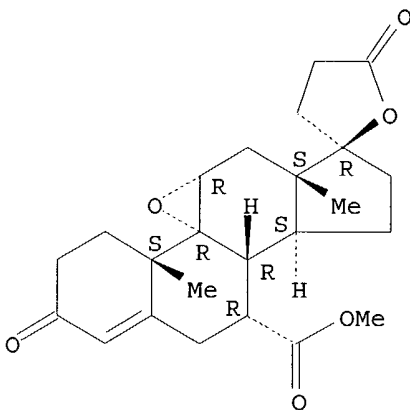
IT 107724-20-9, Eplerenone

RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of aldosterone receptor antagonist to improve cognitive function and treat diseases and improve quality of life)

RN 107724-20-9 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, methyl ester, (7 α ,11 α ,17 α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB Aldosterone receptor antagonists for the prevention and treatment of cognitive dysfunction are disclosed. The compds. of interest are epoxy- and non-epoxy **steroids**. The compds. can also be used to treat heart, kidney, stroke and vascular disease.

L8 ANSWER 19 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:107160 CAPLUS

DOCUMENT NUMBER: 136:161366

TITLE: Epoxy-steroidal aldosterone antagonist and calcium channel blocker combination therapy for treatment of congestive heart failure and other cardiovascular disorders

INVENTOR(S): Schuh, Joseph R.

PATENT ASSIGNEE(S): Pharmacia Corporation, USA

SOURCE: PCT Int. Appl., 231 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

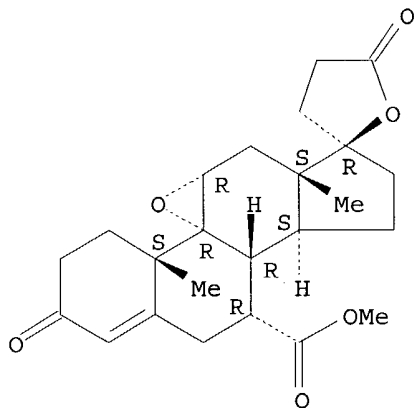
10/608,101

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002009761	A2	20020207	WO 2001-US23677	20010727
WO 2002009761	A3	20030103		
WO 2002009761	C2	20030710		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG EP 1303305 A2 20030423 EP 2001-956001 20010727 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR JP 2004505061 T2 20040219 JP 2002-515313 20010727 US 2003220310 A1 20031127 US 2003-343165 20030127 PRIORITY APPLN. INFO.: US 2000-221359P P 20000727 WO 2001-US23677 W 20010727				
IT 107724-20-9, Eplerenone RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (epoxy-steroidal aldosterone antagonist and calcium channel blocker combination therapy for treatment of congestive heart failure and other cardiovascular disorders) RN 107724-20-9 CAPLUS CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, methyl ester, (7 α ,11 α ,17 α)- (9CI) (CA INDEX NAME)				

Absolute stereochemistry.



IT 395665-48-2 395665-50-6 395665-56-2
 395665-66-4 395665-68-6 396068-70-5
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (epoxy-steroidal aldosterone antagonist and calcium channel blocker combination therapy for treatment of congestive heart failure and other

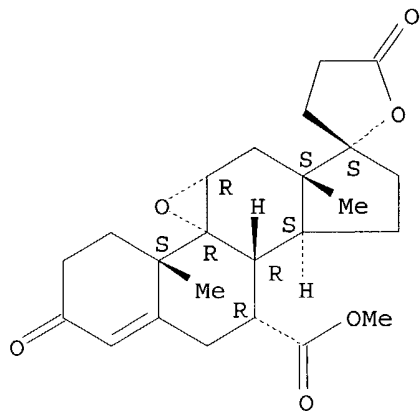
10/608,101

cardiovascular disorders)

RN 395665-48-2 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α)- (9CI) (CA INDEX
NAME)

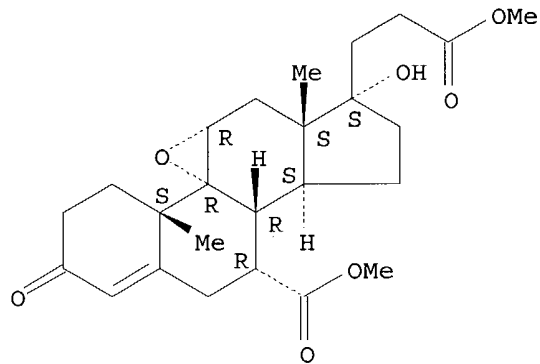
Absolute stereochemistry.



RN 395665-50-6 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, dimethyl
ester, (7 α ,11 α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

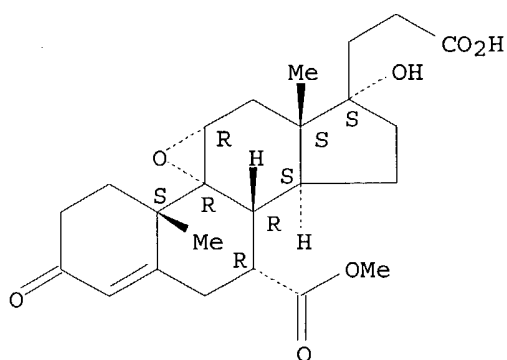


RN 395665-56-2 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-methyl
ester, monopotassium salt, (7 α ,11 α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10/608,101

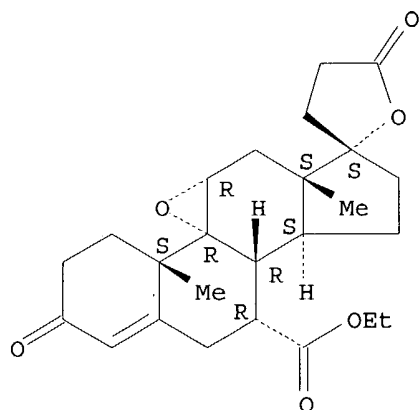


● K

RN 395665-66-4 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, ethyl ester, (7 α ,11 α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

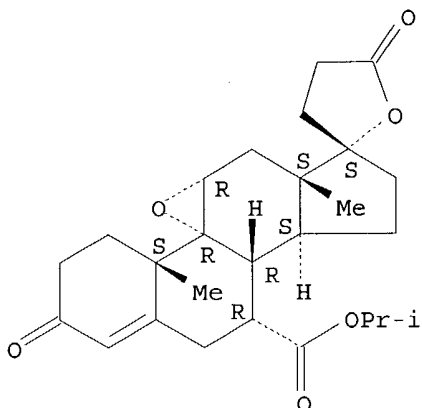


RN 395665-68-6 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, 1-methylethyl ester, (7 α ,11 α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

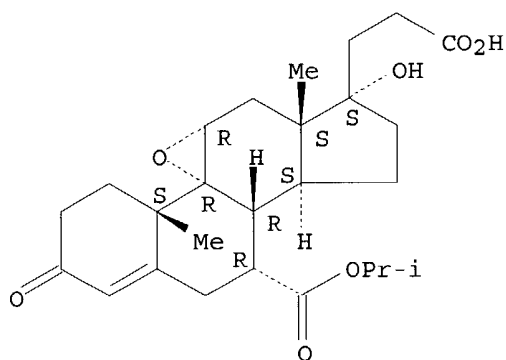
10/608,101



RN 396068-70-5 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
7-(1-methylethyl) ester, monopotassium salt, (7 α ,11 α)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



● K

IT 344450-03-9 344450-04-0 344450-09-5
344450-11-9 396068-72-7 396068-73-8
396068-74-9 396068-75-0 396068-76-1
396068-77-2 396068-78-3 396068-79-4
396068-80-7 396068-81-8 396068-82-9
396068-83-0 396068-84-1 396068-85-2

RL: PRP (Properties)

(epoxy-steroidal aldosterone antagonist and calcium channel blocker
combination therapy for treatment of congestive heart failure and other
cardiovascular disorders)

RN 344450-03-9 CAPLUS

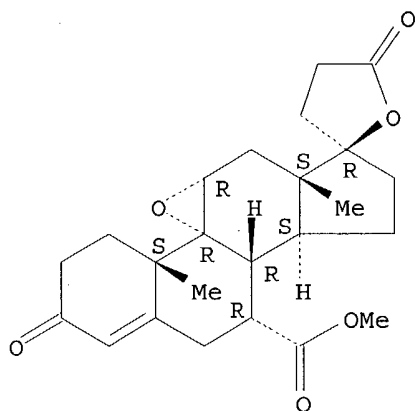
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)-, compd.
with 1,1-dimethylethyl acetate (9CI) (CA INDEX NAME)

CM 1

10/608,101

CRN 107724-20-9
CMF C24 H30 O6

Absolute stereochemistry.



CM 2

CRN 540-88-5
CMF C6 H12 O2

t-Bu-O-Ac

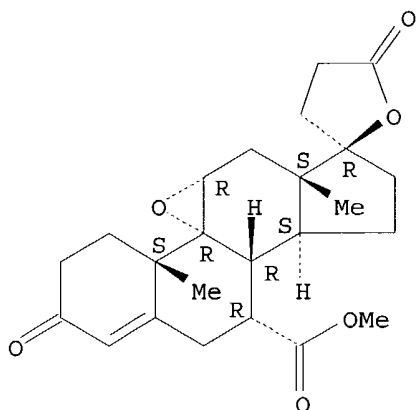
RN 344450-04-0 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with trichloromethane (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9
CMF C24 H30 O6

Absolute stereochemistry.

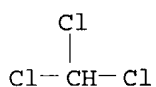
10/608,101



CM 2

CRN 67-66-3

CMF C H Cl3



RN 344450-09-5 CAPLUS

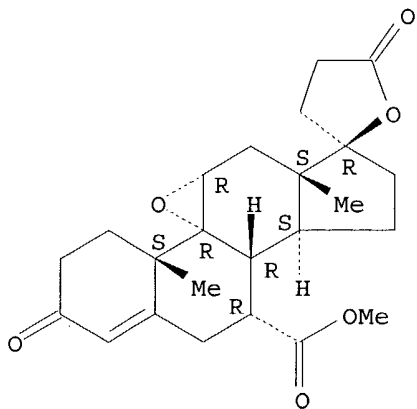
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with 1-octanol (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.



10/608,101

CM 2

CRN 111-87-5

CMF C8 H18 O

HO—(CH₂)₇—Me

RN 344450-11-9 CAPLUS

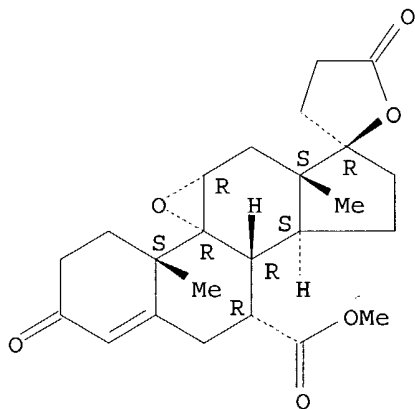
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with 1,2-propanediol (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9

CMF C24 H30 O6

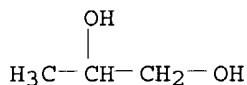
Absolute stereochemistry.



CM 2

CRN 57-55-6

CMF C3 H8 O2



RN 396068-72-7 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with 2-butanone (1:1) (9CI) (CA INDEX NAME)

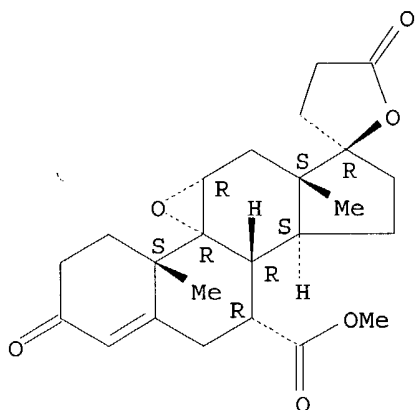
CM 1

CRN 107724-20-9

CMF C24 H30 O6

10/608,101

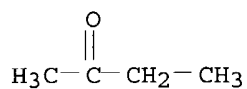
Absolute stereochemistry.



CM 2

CRN 78-93-3

CMF C4 H8 O



RN 396068-73-8 CAPLUS

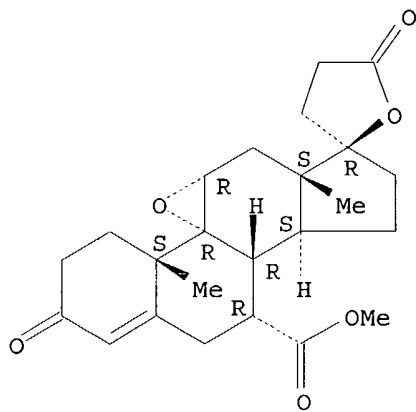
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with 2-propanone (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9

CMF C24 H30 O6

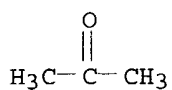
Absolute stereochemistry.



10/608,101

CM 2

CRN 67-64-1
CMF C3 H6 O

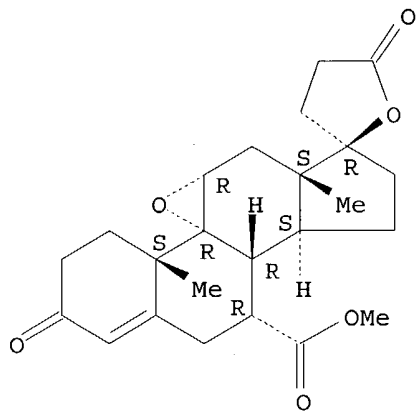


RN 396068-74-9 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with methylbenzene (1:1) (9CI) (CA INDEX NAME)

CM 1

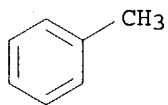
CRN 107724-20-9
CMF C24 H30 O6

Absolute stereochemistry.



CM 2

CRN 108-88-3
CMF C7 H8



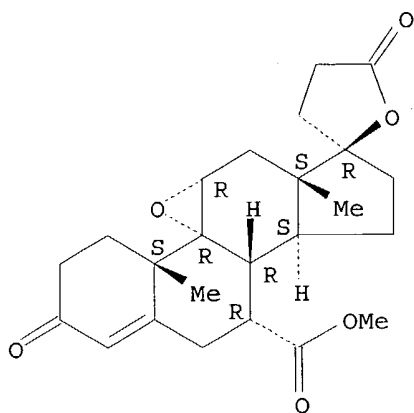
RN 396068-75-0 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with butyl acetate (1:1) (9CI) (CA INDEX NAME)

CM 1

10/608,101

CRN 107724-20-9
CMF C24 H30 O6

Absolute stereochemistry.



CM 2

CRN 123-86-4
CMF C6 H12 O2

n-Bu-O-Ac

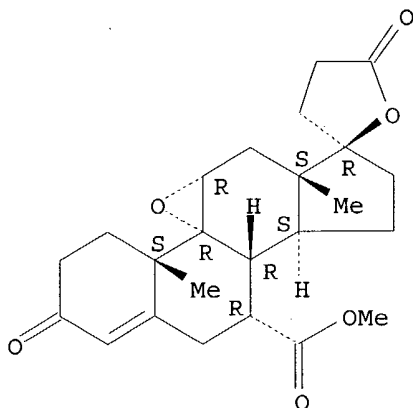
RN 396068-76-1 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with 2-methylpropyl acetate (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9
CMF C24 H30 O6

Absolute stereochemistry.

10/608,101



CM 2

CRN 110-19-0
CMF C6 H12 O2

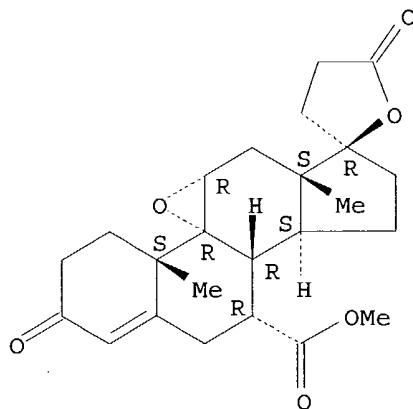
i-Bu-O-Ac

RN 396068-77-2 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with 2-propanol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9
CMF C24 H30 O6

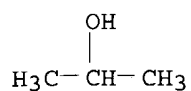
Absolute stereochemistry.



CM 2

10/608,101

CRN 67-63-0
CMF C3 H8 O

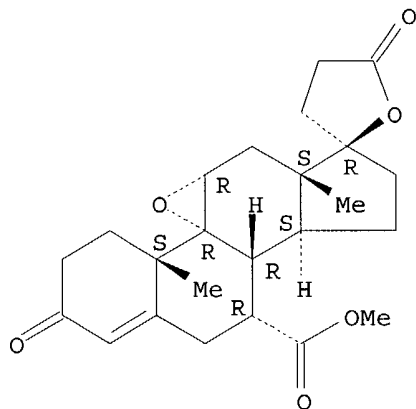


RN 396068-78-3 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with ethanol (1:1) (9CI) (CA INDEX NAME)

CM 1

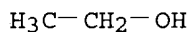
CRN 107724-20-9
CMF C24 H30 O6

Absolute stereochemistry.



CM 2

CRN 64-17-5
CMF C2 H6 O



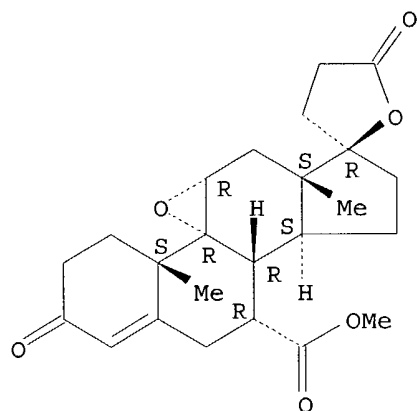
RN 396068-79-4 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with acetic acid (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9
CMF C24 H30 O6

Absolute stereochemistry.

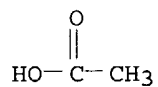
10/608,101



CM 2

CRN 64-19-7

CMF C2 H4 O2



RN 396068-80-7 CAPLUS

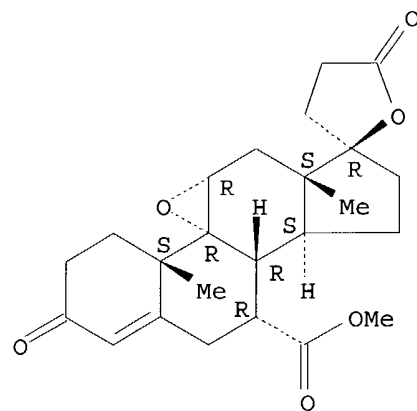
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with methyl acetate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9

CMF C24 H30 O6

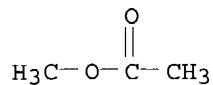
Absolute stereochemistry.



CM 2

10/608,101

CRN 79-20-9
CMF C3 H6 O2

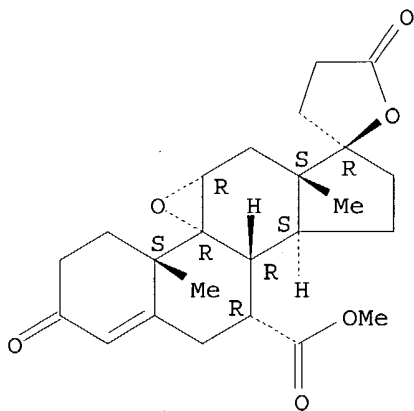


RN 396068-81-8 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with ethyl propanoate (1:1) (9CI) (CA INDEX NAME)

CM 1

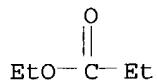
CRN 107724-20-9
CMF C24 H30 O6

Absolute stereochemistry.



CM 2

CRN 105-37-3
CMF C5 H10 O2



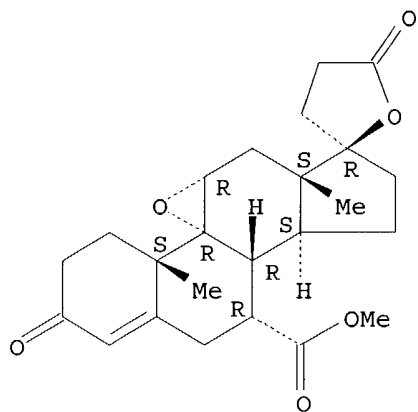
RN 396068-82-9 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with 1-butanol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9
CMF C24 H30 O6

10/608,101

Absolute stereochemistry.



CM 2

CRN 71-36-3
CMF C4 H10 O

$\text{H}_3\text{C}-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{OH}$

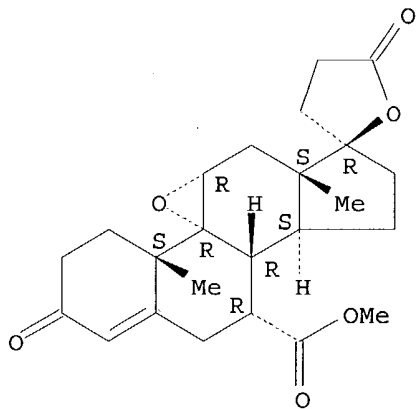
RN 396068-83-0 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)-, compd.
with 1-propanol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9
CMF C24 H30 O6

Absolute stereochemistry.



10/608,101

CM 2

CRN 71-23-8

CMF C3 H8 O

$\text{H}_3\text{C}-\text{CH}_2-\text{CH}_2-\text{OH}$

RN 396068-84-1 CAPLUS

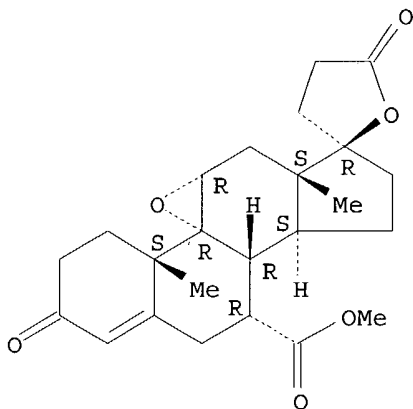
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)-, compd.
with propyl acetate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.



CM 2

CRN 109-60-4

CMF C5 H10 O2

$\text{n-Pr}-\text{O}-\text{Ac}$

RN 396068-85-2 CAPLUS

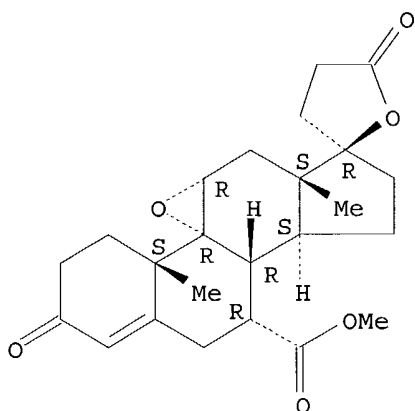
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)-, compd.
with tetrahydrofuran (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.



CM 2

CRN 109-99-9

CMF C4 H8 O



AB A combination therapy comprising a therapeutically effective amount of an epoxy-steroidal aldosterone receptor antagonist and a therapeutically effective amount of a calcium channel blocker is described for treatment of circulatory disorders, including cardiovascular disorders such as hypertension, congestive heart failure, cirrhosis and ascites. Preferred calcium channel blockers are those compds. having high potency and bioavailability. Preferred epoxy-steroidal aldosterone receptor antagonists are 20-spiroxane steroidal compds. characterized by the presence of a $9\alpha,11\alpha$ -substituted epoxy moiety. A preferred combination therapy includes the calcium channel blocker verapamil-HCl and the aldosterone receptor antagonist epoxymexrenone.

L8 ANSWER 20 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:107159 CAPLUS

DOCUMENT NUMBER: 136:172753

TITLE: Epoxy-steroidal aldosterone antagonist and
beta-adrenergic antagonist combination therapy for
treatment of congestive heart failure

INVENTOR(S): Alexander, John C.; Schuh, Joseph R.

PATENT ASSIGNEE(S): Pharmacia Corporation, USA

SOURCE: PCT Int. Appl., 190 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002009760	A2	20020207	WO 2001-US23670	20010727
WO 2002009760	A3	20030123		

10/608,101

WO 2002009760 C2 20030904

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002123485 A1 20020905 US 2001-917403 20010727

EP 1303306 A2 20030423 EP 2001-957290 20010727

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2004511435 T2 20040415 JP 2002-515312 20010727

PRIORITY APPLN. INFO.: US 2000-221365P P 20000727

WO 2001-US23670 W 20010727

IT 344449-96-3

RL: FMU (Formation, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)

(epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist combination therapy for treatment of congestive heart failure)

RN 344449-96-3 CAPLUS

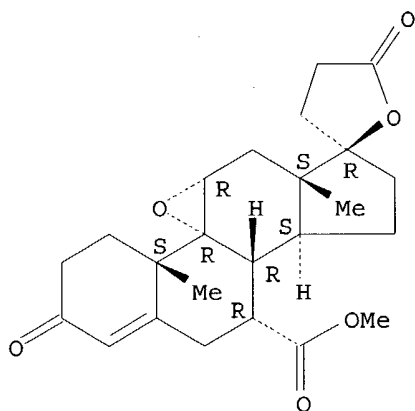
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, methyl ester, (7 α ,11 α ,17 α)-, compd. with 2-butanone (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.

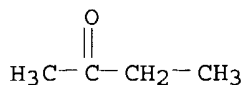


CM 2

CRN 78-93-3

CMF C4 H8 O

10/608,101



IT 107724-20-9, Eplerenone

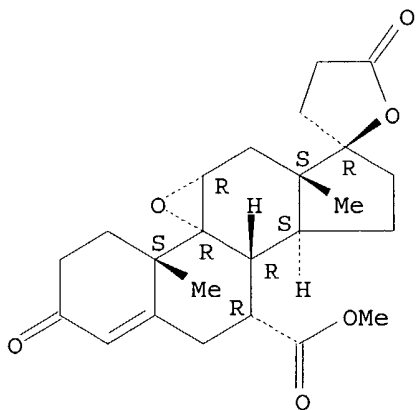
RL: PAC (Pharmacological activity); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist combination therapy for treatment of congestive heart failure)

RN 107724-20-9 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



IT 395665-48-2 395665-50-6 395665-54-0

395665-56-2 395665-66-4 395665-68-6

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

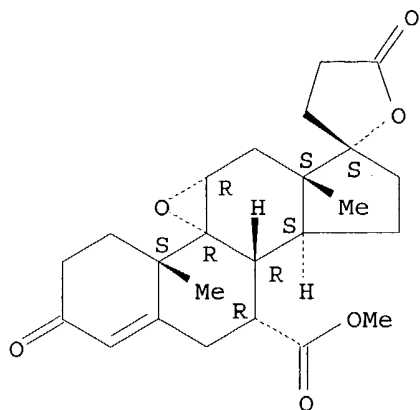
(epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist combination therapy for treatment of congestive heart failure)

RN 395665-48-2 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α)- (9CI) (CA INDEX
NAME)

Absolute stereochemistry.

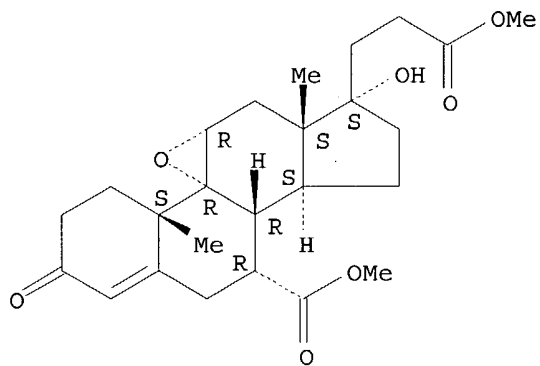
10/608,101



RN 395665-50-6 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, dimethyl ester, (7 α ,11 α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

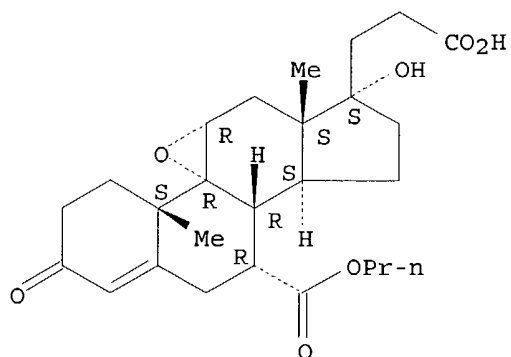


RN 395665-54-0 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-propyl ester, monopotassium salt, (7 α ,11 α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10/608,101

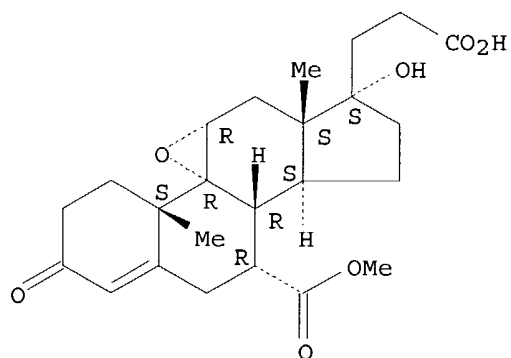


● K

RN 395665-56-2 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-methyl ester, monopotassium salt, (7 α ,11 α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

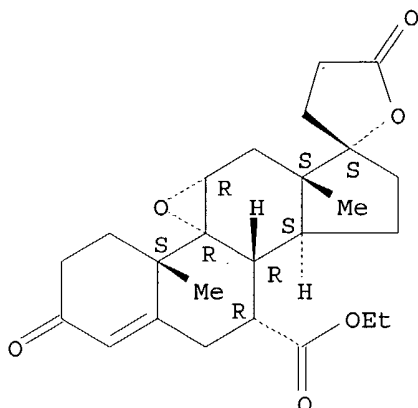


● K

RN 395665-66-4 CAPLUS

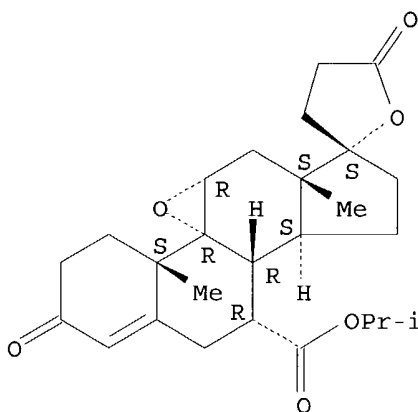
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, ethyl ester, (7 α ,11 α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 395665-68-6 CAPLUS
 CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ-lactone, 1-methylethyl ester, (7α,11α)- (9CI) (CA
 INDEX NAME)

Absolute stereochemistry.



AB A combination therapy comprising a therapeutically-effective amount of an epoxy-steroidal aldosterone receptor antagonist and a therapeutically-effective amount of a beta-adrenergic antagonist is described for treatment of circulatory disorders, including cardiovascular disorders such as hypertension, congestive heart failure, cirrhosis and ascites. Preferred beta-adrenergic antagonists are those compds. having high potency and bioavailability. Preferred epoxy-steroidal aldosterone receptor antagonists are 20-spiroxane steroidal compds. characterized by the presence of a 9α, 11α-substituted epoxy moiety. A preferred combination therapy includes the beta-adrenergic antagonist metoprolol succinate and the aldosterone receptor antagonist epoxymexrenone. Crystal forms of eplerenone were prepared as well as the Me Et ketone solvate.

L8 ANSWER 21 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2002:107158 CAPLUS
 DOCUMENT NUMBER: 136:161365
 TITLE: Aldosterone antagonist-cyclooxygenase-2 inhibitor
 combination therapy to prevent or treat

INVENTOR(S): inflammation-related cardiovascular disorders
 Rocha, Ricardo; Zack, Marc D.; McMahon, Ellen G.
 PATENT ASSIGNEE(S): Pharmacia Corporation, USA
 SOURCE: PCT Int. Appl., 273 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 6
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002009759	A2	20020207	WO 2001-US23601	20010726
WO 2002009759	A3	20021128		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1303308	A2	20030423	EP 2001-961746	20010726
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003125312	A1	20030703	US 2001-915784	20010726
US 6716829	B2	20040406		
JP 2004505060	T2	20040219	JP 2002-515311	20010726
US 2003191100	A1	20031009	US 2002-243876	20020913
PRIORITY APPLN. INFO.:				
US 2000-221364P P 20000727				
US 2001-261497P P 20010112				
US 1999-164390P P 19991109				
US 2000-211064P P 20000613				
US 2000-211250P P 20000613				
US 2000-211253P P 20000613				
US 2000-211264P P 20000613				
US 2000-211311P P 20000613				
US 2000-211340P P 20000613				
US 2000-211451P P 20000613				
US 2000-211459P P 20000613				
US 2000-221358P P 20000727				
US 2000-233056P P 20000914				
US 2000-709253 A2 20001108				
US 2000-712543 A1 20001114				
US 2001-261352P P 20010112				
WO 2001-US23601 W 20010726				

OTHER SOURCE(S): MARPAT 136:161365

IT 396068-72-7P

RL: PNU (Preparation, unclassified); PRP (Properties); PREP (Preparation)
 (aldosterone antagonist-cyclooxygenase-2 inhibitor combination therapy
 to prevent or treat inflammation-related cardiovascular 1)

RN 396068-72-7 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)-, compd.
 with 2-butanone (1:1) (9CI) (CA INDEX NAME)

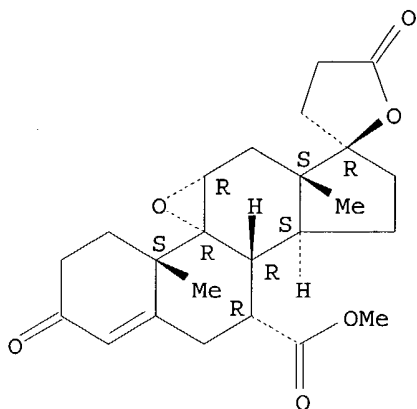
CM 1

CRN 107724-20-9

10/608,101

CMF C24 H30 O6

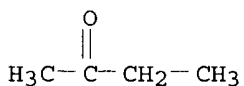
Absolute stereochemistry.



CM 2

CRN 78-93-3

CMF C4 H8 O



IT 107724-20-9

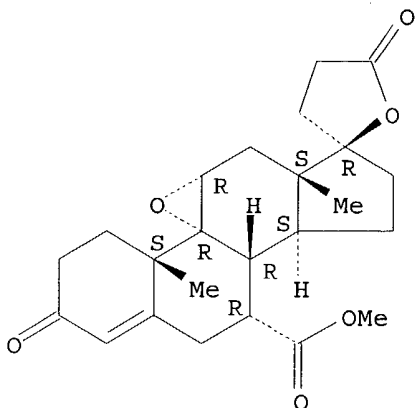
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(aldosterone antagonist-cyclooxygenase-2 inhibitor combination therapy to prevent or treat inflammation-related cardiovascular disorders)

RN 107724-20-9 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ-lactone, methyl ester, (7α,11α,17α)- (9CI) (CA
 INDEX NAME)

Absolute stereochemistry.



IT 95716-76-0 95716-78-2 95716-98-6

95716-99-7 95717-02-5

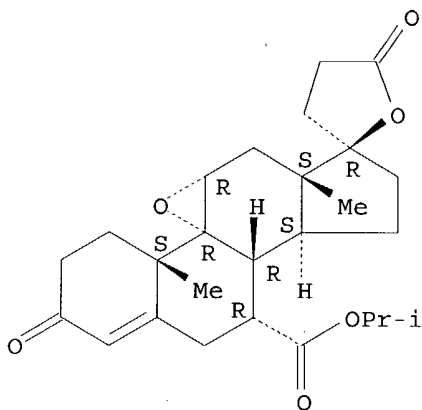
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(aldosterone antagonist-cyclooxygenase-2 inhibitor combination therapy
to prevent or treat inflammation-related cardiovascular disorders)

RN 95716-76-0 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, 1-methylethyl ester, (7α,11α,17α)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

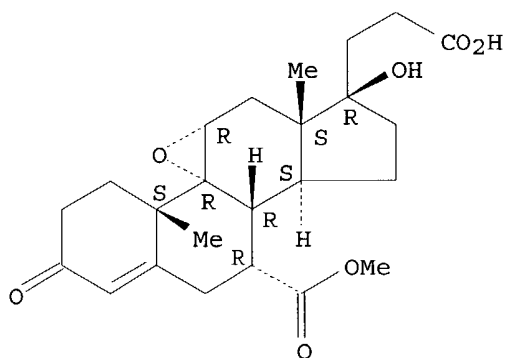


RN . 95716-78-2 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, ethyl ester, (7α,11α,17α)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry. Rotation (+).

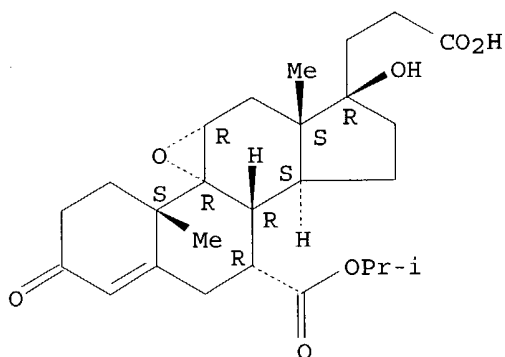
Absolute stereochemistry.



RN	95716-99-7	CAPLUS
CN	Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-(1-methylethyl) ester, monopotassium salt, (7 α ,11 α ,17 α)- (9CI) (CA INDEX NAME)	

Page 113

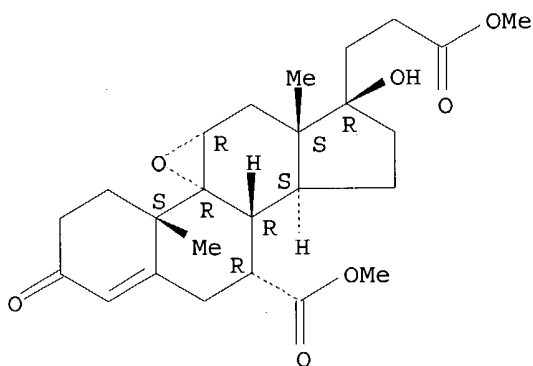
10/608,101



● K

RN 95717-02-5 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, dimethyl ester, (7 α ,11 α ,17 α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 344450-01-7 344450-03-9 344450-04-0
344450-09-5 344450-11-9 396068-73-8
396068-74-9 396068-76-1 396068-77-2
396068-78-3 396068-79-4 396068-80-7
396068-81-8 396068-82-9 396068-83-0
396068-84-1 396068-85-2

RL: PRP (Properties)

(aldosterone antagonist-cyclooxygenase-2 inhibitor combination therapy
to prevent or treat inflammation-related cardiovascular disorders)

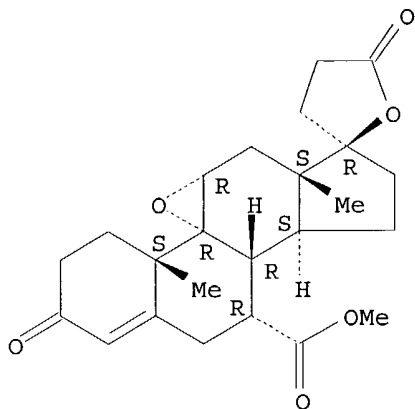
RN 344450-01-7 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)-, compd.
with butyl acetate (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9
CMF C24 H30 O6

10/608,101

Absolute stereochemistry.



CM 2

CRN 123-86-4

CMF C6 H12 O2

n-Bu-O-Ac

RN 344450-03-9 CAPLUS

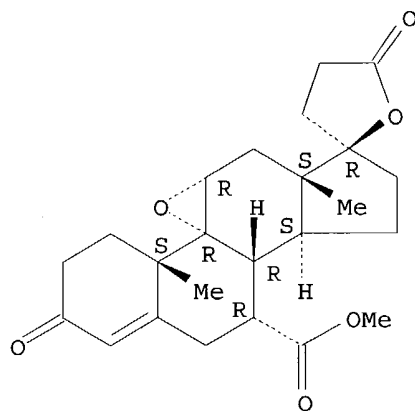
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with 1,1-dimethylethyl acetate (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.



CM 2

10/608,101

CRN 540-88-5
CMF C6 H12 O2

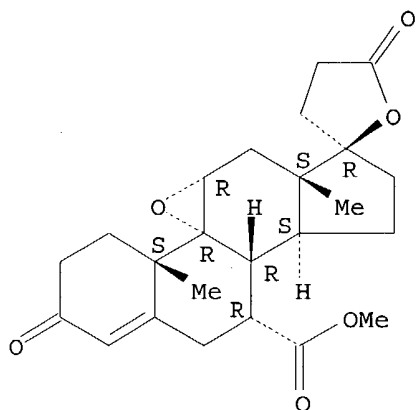
t-Bu-O-Ac

RN 344450-04-0 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with trichloromethane (9CI) (CA INDEX NAME)

CM 1

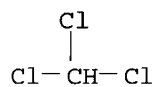
CRN 107724-20-9
CMF C24 H30 O6

Absolute stereochemistry.



CM 2

CRN 67-66-3
CMF C H Cl3



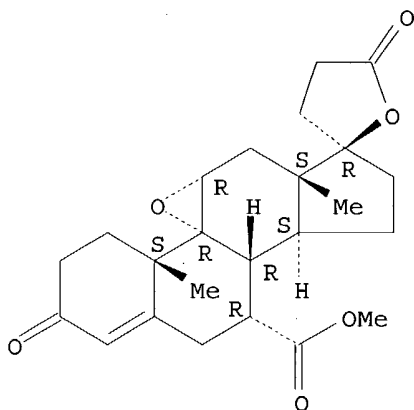
RN 344450-09-5 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with 1-octanol (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9
CMF C24 H30 O6

Absolute stereochemistry.

10/608,101



CM 2

CRN 111-87-5

CMF C8 H18 O

HO-(CH₂)₇-Me

RN 344450-11-9 CAPLUS

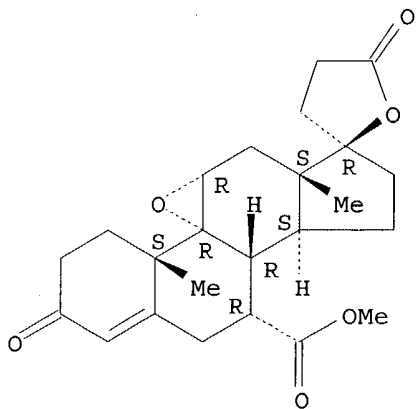
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with 1,2-propanediol (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9

CMF C24 H30 O6

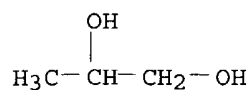
Absolute stereochemistry.



CM 2

10/608,101

CRN 57-55-6
CMF C3 H8 O2

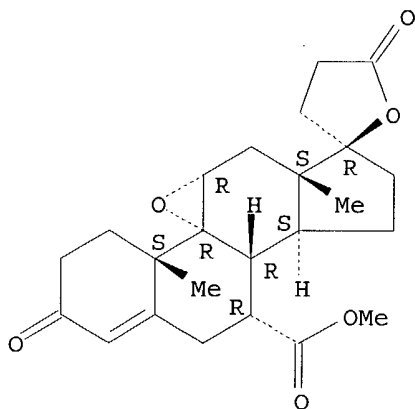


RN 396068-73-8 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with 2-propanone (1:1) (9CI) (CA INDEX NAME)

CM 1

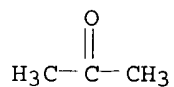
CRN 107724-20-9
CMF C24 H30 O6

Absolute stereochemistry.



CM 2

CRN 67-64-1
CMF C3 H6 O



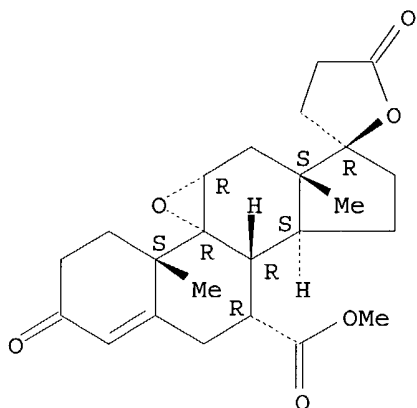
RN 396068-74-9 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with methylbenzene (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9
CMF C24 H30 O6

10/608,101

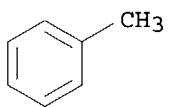
Absolute stereochemistry.



CM 2

CRN 108-88-3

CMF C7 H8



RN 396068-76-1 CAPLUS

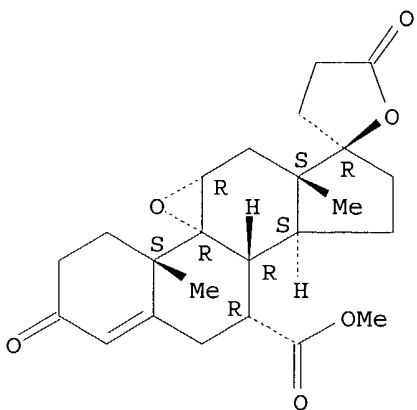
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
gamma-lactone, methyl ester, (7alpha,11alpha,17alpha)-, compd.
with 2-methylpropyl acetate (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.



10/608,101

CM 2

CRN 110-19-0
CMF C6 H12 O2

i-Bu-O-Ac

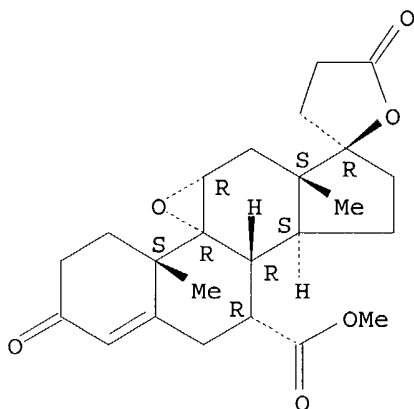
RN 396068-77-2 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with 2-propanol (1:1) (9CI) (CA INDEX NAME)

CM 1

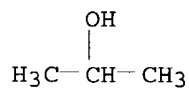
CRN 107724-20-9
CMF C24 H30 O6

Absolute stereochemistry.



CM 2

CRN 67-63-0
CMF C3 H8 O



RN 396068-78-3 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with ethanol (1:1) (9CI) (CA INDEX NAME)

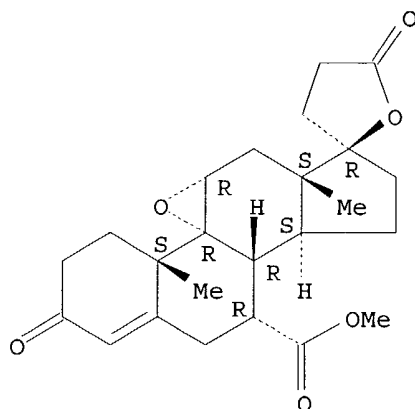
CM 1

CRN 107724-20-9

10/608,101

CMF C24 H30 O6

Absolute stereochemistry.



CM 2

CRN 64-17-5

CMF C2 H6 O

H₃C-CH₂-OH

RN 396068-79-4 CAPLUS

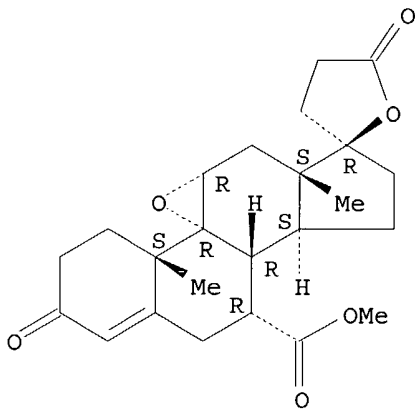
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with acetic acid (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9

CMF C24 H30 O6

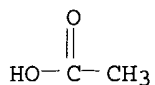
Absolute stereochemistry.



10/608,101

CM 2

CRN 64-19-7
CMF C2 H4 O2



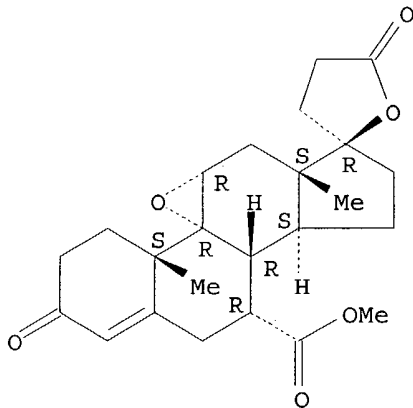
RN 396068-80-7 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with methyl acetate (1:1) (9CI) (CA INDEX NAME)

CM 1

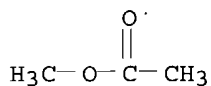
CRN 107724-20-9
CMF C24 H30 O6

Absolute stereochemistry.



CM 2

CRN 79-20-9
CMF C3 H6 O2



RN 396068-81-8 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with ethyl propanoate (1:1) (9CI) (CA INDEX NAME)

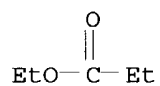
CM 1

CRN 107724-20-9
CMF C24 H30 O6

The chemical structure shows a complex polycyclic molecule, likely a steroid derivative. It features a central four-ring core. A ketone group (C=O) is attached to the leftmost ring. A methyl group (Me) is attached to the second ring from the left. A methoxy group (OMe) is attached to the third ring from the left. The rightmost ring is a five-membered ring with a ketone group (C=O) and a methyl group (Me). Stereochemistry is indicated with wedges and dashes for the methyl groups and hydrogens. The structure is labeled with 'R' and 'S' at various positions, indicating stereochemical centers.

CM 2

CRN 105-37-3
CMF C5 H10 O2



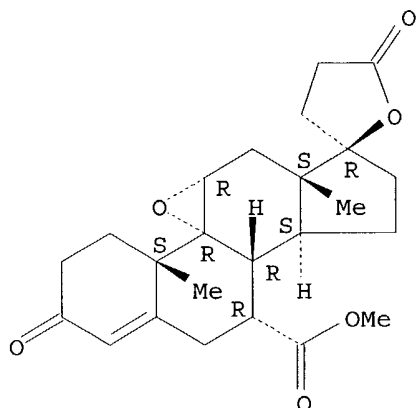
RN	396068-82-9	CAPLUS
CN	Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ-lactone, methyl ester, (7α,11α,17α)-, compd. with 1-butanol (1:1) (9CI) (CA INDEX NAME)	

CM 1

CRN 107724-20-9
CMF C24 H30 O6

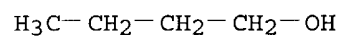
Page 123

10/608,101



CM 2

CRN 71-36-3
CMF C4 H10 O



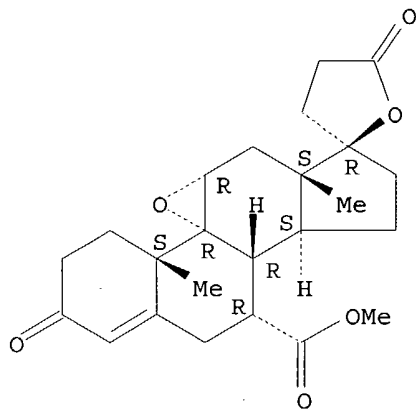
RN 396068-83-0 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with 1-propanol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9
CMF C24 H30 O6

Absolute stereochemistry.



CM 2

10/608,101

CRN 71-23-8
CMF C3 H8 O

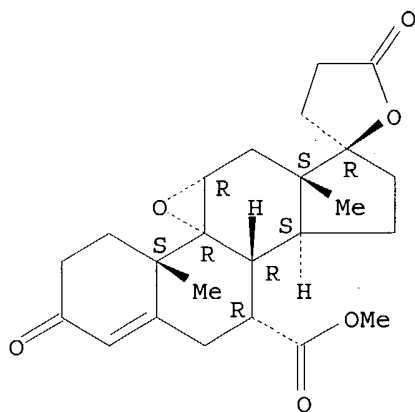
$\text{H}_3\text{C}-\text{CH}_2-\text{CH}_2-\text{OH}$

RN 396068-84-1 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)-, compd.
with propyl acetate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9
CMF C24 H30 O6

Absolute stereochemistry.



CM 2

CRN 109-60-4
CMF C5 H10 O2

$\text{n-Pr}-\text{O}-\text{Ac}$

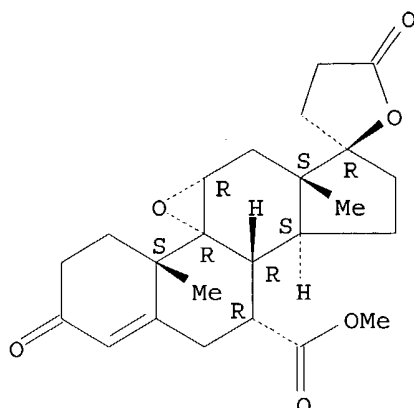
RN 396068-85-2 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)-, compd.
with tetrahydrofuran (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9
CMF C24 H30 O6

Absolute stereochemistry.

10/608,101



CM 2

CRN 109-99-9

CMF C4 H8 O



AB Combinations of aldosterone blockers and Cyclooxygenase-2 inhibitors useful in the treatment of inflammation-related cardiovascular disorders are disclosed.

L8 ANSWER 22 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:107086 CAPLUS

DOCUMENT NUMBER: 136:161353

TITLE: Aldosterone blocker therapy to prevent or treat inflammation-related disorders

INVENTOR(S): Rocha, Richardo; Zack, Marc D.; McMahon, Ellen G.; Blasi, Eileen R.

PATENT ASSIGNEE(S): Pharmacia Corporation, USA

SOURCE: PCT Int. Appl., 210 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002009683	A2	20020207	WO 2001-US23520	20010726
WO 2002009683	C2	20030612		
WO 2002009683	A3	20030912		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

10/608,101

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
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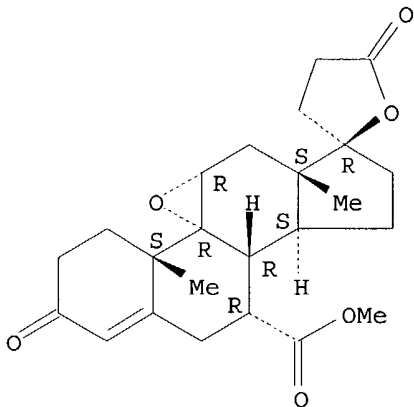
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US 6716829	B2	20040406		
US 2003162759	A1	20030828	US 2001-916136	20010726
EP 1368009	A2	20031210	EP 2001-959222	20010726
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004518611	T2	20040624	JP 2002-515236	20010726
US 2003191100	A1	20031009	US 2002-243876	20020913
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			US 2000-221358P	P 20000727
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			US 2000-712543	A1 20001114
			US 2001-261497P	P 20010112
			WO 2001-US23520	W 20010726

IT 107724-20-9, Eplerenone
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adosterone blocker therapy to prevent or treat inflammation-related disorder)

RN 107724-20-9 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



IT 95716-76-0 95716-78-2 95716-98-6
95716-99-7 95717-02-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

10/608,101

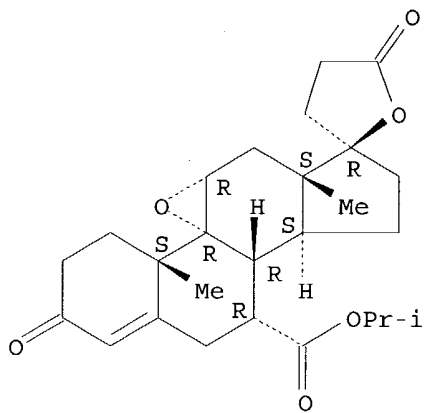
(Biological study); USES (Uses)

(adosterone blocker therapy to prevent or treat inflammation-related disorder)

RN 95716-76-0 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, 1-methylethyl ester, (7 α ,11 α ,17 α)-
(9CI) (CA INDEX NAME)

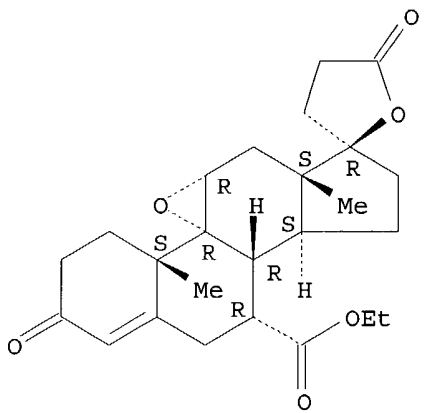
Absolute stereochemistry. Rotation (-).



RN 95716-78-2 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, ethyl ester, (7 α ,11 α ,17 α)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry. Rotation (+).

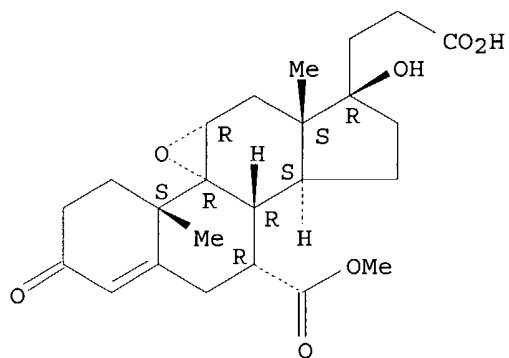


RN 95716-98-6 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-methyl
ester, monopotassium salt, (7 α ,11 α ,17 α)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

10/608,101

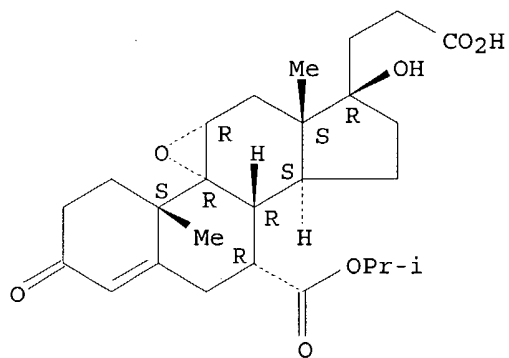


● K

RN 95716-99-7 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
7-(1-methylethyl) ester, monopotassium salt, (7 α ,11 α ,17 α) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



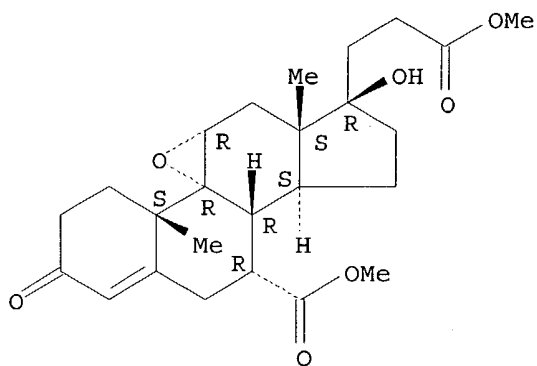
● K

RN 95717-02-5 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, dimethyl
ester, (7 α ,11 α ,17 α) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10/608,101



IT 344450-03-9 344450-04-0 344450-09-5
344450-11-9 396068-72-7 396068-73-8
396068-74-9 396068-76-1 396068-77-2
396068-78-3 396068-79-4 396068-80-7
396068-81-8 396068-82-9 396068-83-0
396068-84-1 396068-85-2 396077-49-9

RL: PRP (Properties)
(adosterone blocker therapy to prevent or treat inflammation-related disorder)

RN 344450-03-9 CAPLUS

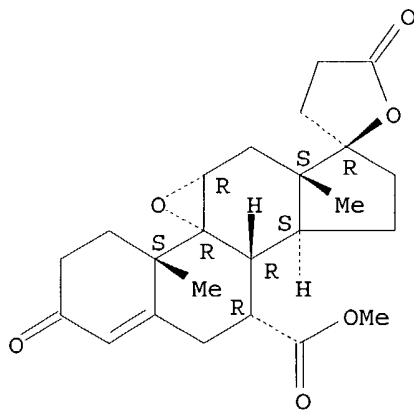
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)-, compd.
with 1,1-dimethylethyl acetate (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.



CM 2

CRN 540-88-5

CMF C6 H12 O2

10/608,101

t-Bu-O-Ac

RN 344450-04-0 CAPLUS

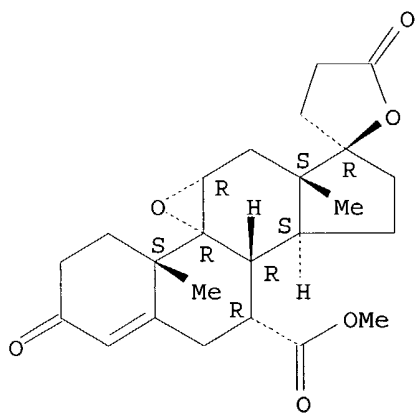
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with trichloromethane (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9

CMF C24 H30 O6

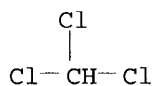
Absolute stereochemistry.



CM 2

CRN 67-66-3

CMF C H Cl3



RN 344450-09-5 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with 1-octanol (9CI) (CA INDEX NAME)

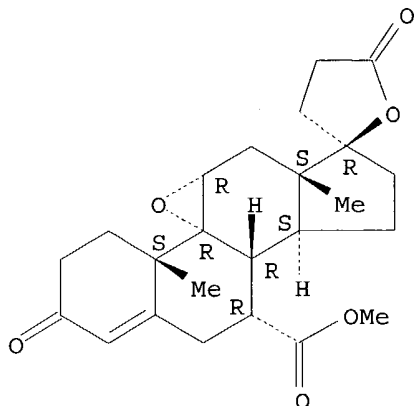
CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.

10/608,101



CM 2

CRN 111-87-5

CMF C8 H18 O

HO-(CH₂)₇-Me

RN 344450-11-9 CAPLUS

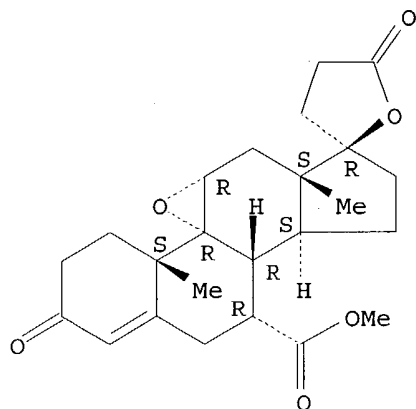
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with 1,2-propanediol (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9

CMF C24 H30 O6

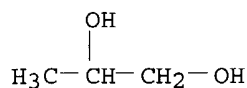
Absolute stereochemistry.



CM 2

10/608,101

CRN 57-55-6
CMF C3 H8 O2

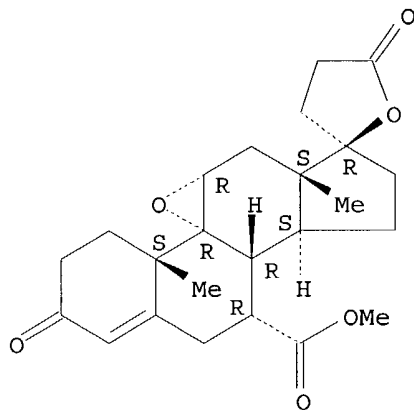


RN 396068-72-7 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with 2-butanone (1:1) (9CI) (CA INDEX NAME)

CM 1

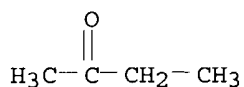
CRN 107724-20-9
CMF C24 H30 O6

Absolute stereochemistry.



CM 2

CRN 78-93-3
CMF C4 H8 O



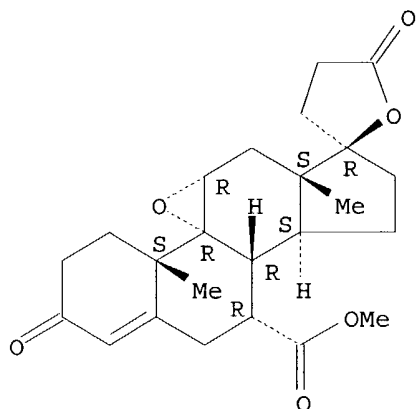
RN 396068-73-8 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with 2-propanone (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9
CMF C24 H30 O6

10/608,101

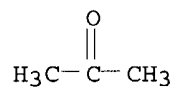
Absolute stereochemistry.



CM 2

CRN 67-64-1

CMF C3 H6 O



RN 396068-74-9 CAPLUS

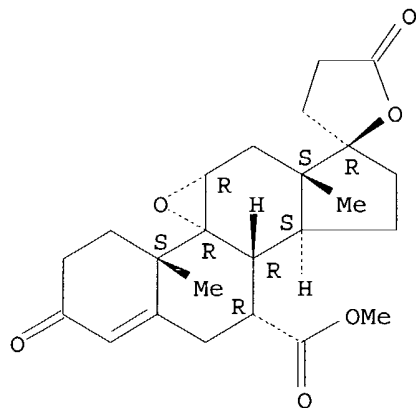
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with methylbenzene (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.

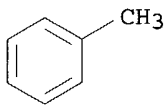


10/608,101

CM 2

CRN 108-88-3

CMF C7 H8



RN 396068-76-1 CAPLUS

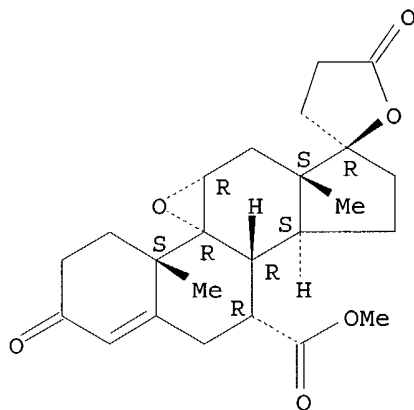
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)-, compd.
with 2-methylpropyl acetate (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.



CM 2

CRN 110-19-0

CMF C6 H12 O2

i-Bu-O-Ac

RN 396068-77-2 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)-, compd.
with 2-propanol (1:1) (9CI) (CA INDEX NAME)

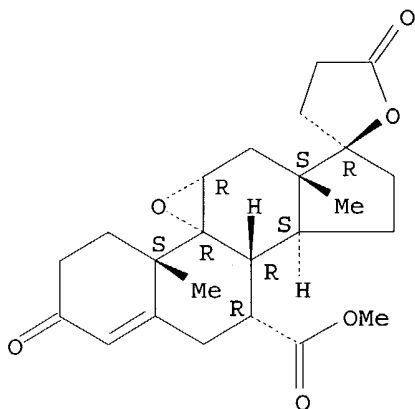
CM 1

CRN 107724-20-9

10/608,101

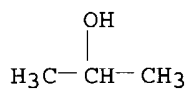
CMF C24 H30 O6

Absolute stereochemistry.



CM. 2

CRN 67-63-0

C3H8O

RN 396068-78-3 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ-lactone, methyl ester, (7α,11α,17α)-, compd.
 with ethanol (1:1) (9CI) (CA INDEX NAME)

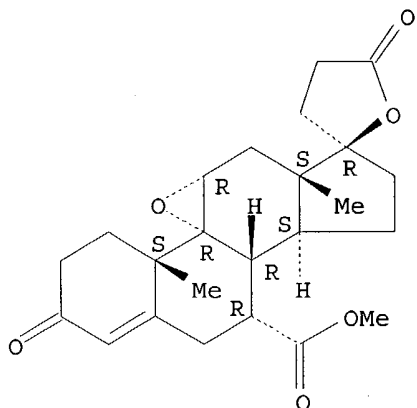
CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.

10/608,101



CM 2

CRN 64-17-5

CMF C2 H6 O

$\text{H}_3\text{C}-\text{CH}_2-\text{OH}$

RN 396068-79-4 CAPLUS

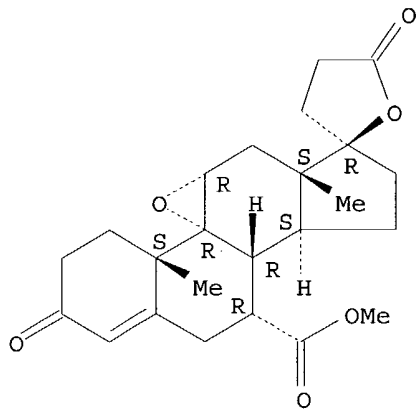
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with acetic acid (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9

CMF C24 H30 O6

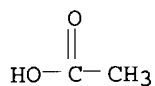
Absolute stereochemistry.



CM 2

10/608,101

CRN 64-19-7
CMF C2 H4 O2

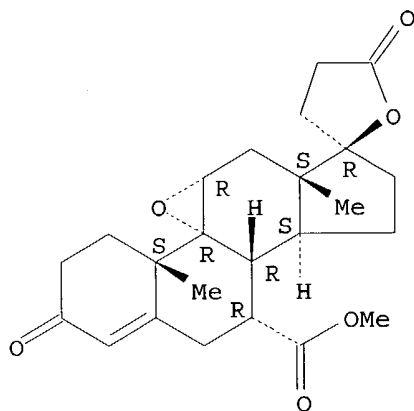


RN 396068-80-7 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with methyl acetate (1:1) (9CI) (CA INDEX NAME)

CM 1

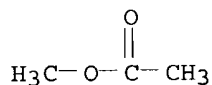
CRN 107724-20-9
CMF C24 H30 O6

Absolute stereochemistry.



CM 2

CRN 79-20-9
CMF C3 H6 O2

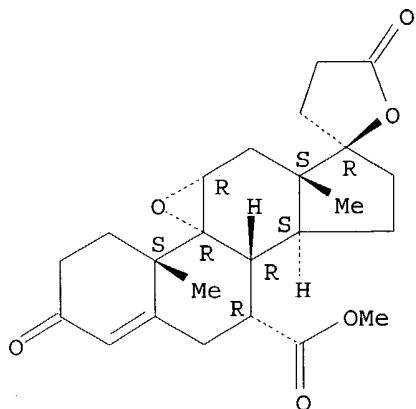


RN 396068-81-8 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with ethyl propanoate (1:1) (9CI) (CA INDEX NAME)

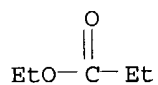
CM 1

CRN 107724-20-9
CMF C24 H30 O6

Absolute stereochemistry.

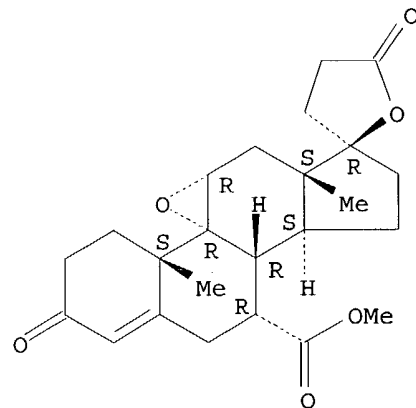


CRN 105-37-3
CMF C5 H10 O2



CRN 107724-20-9
CMF C24 H30 O6

Absolute stereochemistry.



10/608,101

CM 2

CRN 71-36-3

CMF C4 H10 O

H₃C-CH₂-CH₂-CH₂-OH

RN 396068-83-0 CAPLUS

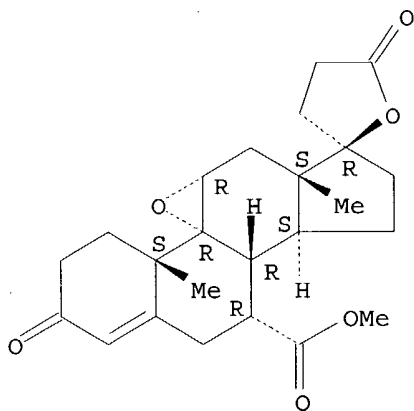
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with 1-propanol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.



CM 2

CRN 71-23-8

CMF C3 H8 O

H₃C-CH₂-CH₂-OH

RN 396068-84-1 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with propyl acetate (1:1) (9CI) (CA INDEX NAME)

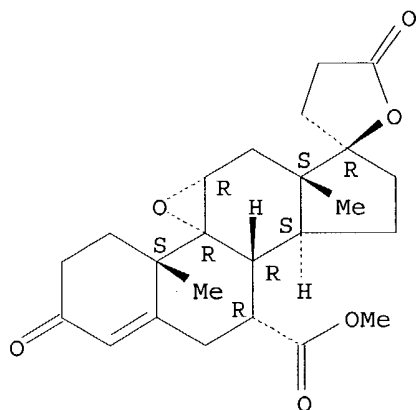
CM 1

CRN 107724-20-9

CMF C24 H30 O6

Absolute stereochemistry.

10/608,101



CM 2

CRN 109-60-4
CMF C5 H10 O2

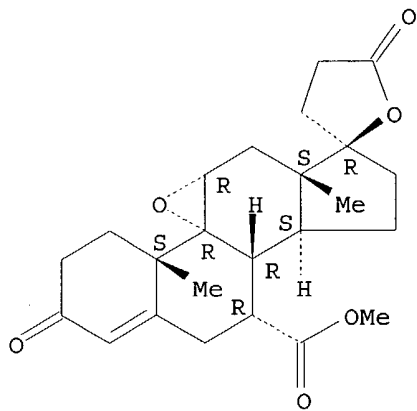
n-Pr-O-Ac

RN 396068-85-2 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with tetrahydrofuran (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9
CMF C24 H30 O6

Absolute stereochemistry.



CM 2

10/608,101

CRN 109-99-9
CMF C4 H8 O

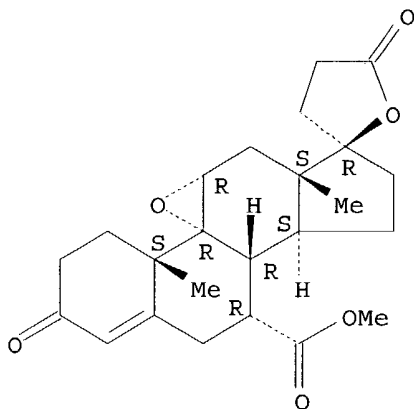


RN 396077-49-9 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)-, compd.
with butyl acetate (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107724-20-9
CMF C24 H30 O6

Absolute stereochemistry.



CM 2

CRN 123-86-4
CMF C6 H12 O2

n-Bu-O-Ac

AB Aldosterone blockers used for the treatment and prevention of inflammation are disclosed.

L8 ANSWER 23 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:923600 CAPLUS

DOCUMENT NUMBER: 136:31688

TITLE: Use of an epoxy-steroidal aldosterone antagonist for the treatment or prophylaxis of aldosterone-mediated pathogenic effects

INVENTOR(S): Williams, Gordon H.; Funder, John W.; Garthwaite, Susan M.; Roniker, Barbara; Fedde, Kenton N.; Rocha, Ricardo

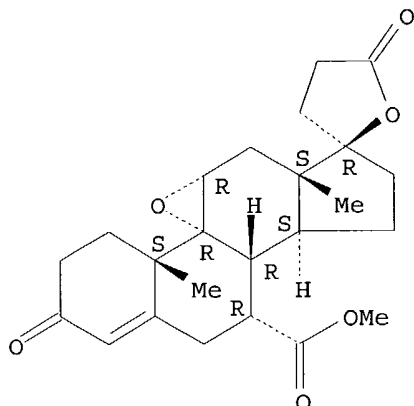
10/608,101

PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 318 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001095893	A1	20011220	WO 2000-US31263	20001114
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
US 2003125312	A1	20030703	US 2001-915784	20010726
US 6716829	B2	20040406		
US 2003191100	A1	20031009	US 2002-243876	20020913
PRIORITY APPLN. INFO.:			US 2000-211064P	P 20000613
			US 2000-211250P	P 20000613
			US 2000-211253P	P 20000613
			US 2000-211264P	P 20000613
			US 2000-211311P	P 20000613
			US 2000-211340P	P 20000613
			US 2000-211451P	P 20000613
			US 2000-211459P	P 20000613
			US 2000-221358P	P 20000727
			US 2000-221364P	P 20000727
			US 2000-233056P	P 20000914
			US 1999-164390P	P 19991109
			US 2000-709253	A2 20001108
			US 2000-712543	A1 20001114
			US 2001-261352P	P 20010112
			US 2001-261497P	P 20010112

IT 107724-20-9DP, Eplerenone, derivs.
RL: PAC (Pharmacological activity); PEP (Physical, engineering or chemical process); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(antihypertensive, renal, and metabolic effects of eplerenone and enalapril in patients with type 2 diabetes, albuminuria, and hypertension)
RN 107724-20-9 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, methyl ester, (7 α ,11 α ,17 α)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **107724-20-9P**, Eplerenone

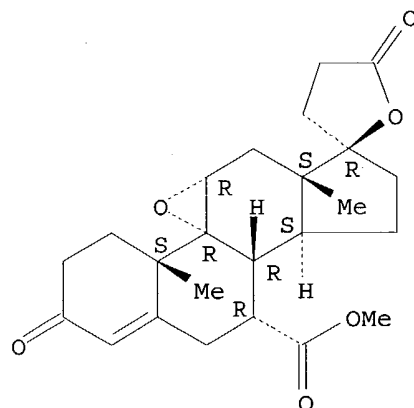
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(use of epoxy-steroidal aldosterone antagonist for treatment or prophylaxis of aldosterone-mediated pathogenic effects)

RN 107724-20-9 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, methyl ester, (7 α ,11 α ,17 α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **95716-76-0P 95716-78-2P 95716-98-6P**

95716-99-7P 95717-02-5P

RL: PAC (Pharmacological activity); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

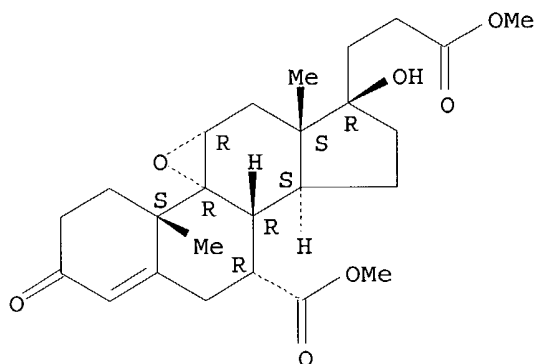
(use of epoxy-steroidal aldosterone antagonist for treatment or prophylaxis of aldosterone-mediated pathogenic effects)

RN 95716-76-0 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, 1-methylethyl ester, (7 α ,11 α ,17 α)- (9CI) (CA INDEX NAME)

-k

—**CA**



AB The present invention provides methods for the treatment or prophylaxis of one or more aldosterone-mediated pathogenic effects in a subject suffering from or susceptible to the pathogenic effect or effects wherein the subject has one or more conditions selected from the group consisting of a sub-normal endogenous aldosterone level, salt sensitivity and an elevated dietary sodium intake. The methods comprise administering to the subject a therapeutically-effective amount of one or more epoxy-steroidal compds. that are aldosterone antagonists. The epoxy-steroidal compds. can be administered as solvated or nonsolvated crystals or in an amorphous form. In addition to use of the epoxy-steroidal compds., their formulation and crystallization are exemplified.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 24 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:923599 CAPLUS

DOCUMENT NUMBER: 136:31687

TITLE: Use of an aldosterone antagonist, specifically a spirolactone-type steroidal compound, for the treatment or prophylaxis of aldosterone-mediated pathogenic effects

INVENTOR(S): Williams, Gordon H.; Funder, John W.; Garthwaite, Susan M.; Roniker, Barbara; Fedde, Kenton N.; Rocha, Ricardo

PATENT ASSIGNEE(S): Pharmacia Corporation, USA

SOURCE: PCT Int. Appl., 329 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001095892	A1	20011220	WO 2000-US31155	20001114
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

EP 1289507	A1	20030312	EP 2000-978588	20001114
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004503495	T2	20040205	JP 2002-510071	20001114
US 2003125312	A1	20030703	US 2001-915784	20010726
US 6716829	B2	20040406		
US 2003191100	A1	20031009	US 2002-243876	20020913
PRIORITY APPLN. INFO.:			US 2000-211064P	P 20000613
			US 2000-211250P	P 20000613
			US 2000-211253P	P 20000613
			US 2000-211264P	P 20000613
			US 2000-211311P	P 20000613
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			US 2000-233056P	P 20000914
			US 1999-164390P	P 19991109
			US 2000-709253	A2 20001108
			US 2000-712543	A1 20001114
			WO 2000-US31155	W 20001114
			US 2001-261352P	P 20010112
			US 2001-261497P	P 20010112

IT 107724-20-9P, Eplerenone

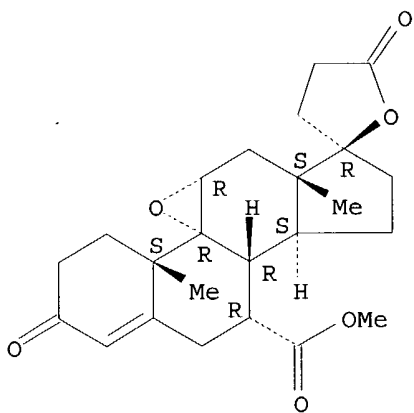
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(use of aldosterone antagonist for treatment or prophylaxis of aldosterone-mediated pathogenic effects)

RN 107724-20-9 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, methyl ester, (7 α ,11 α ,17 α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 107724-20-9DP, Eplerenone, derivs.

RL: PAC (Pharmacological activity); PEP (Physical, engineering or chemical process); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

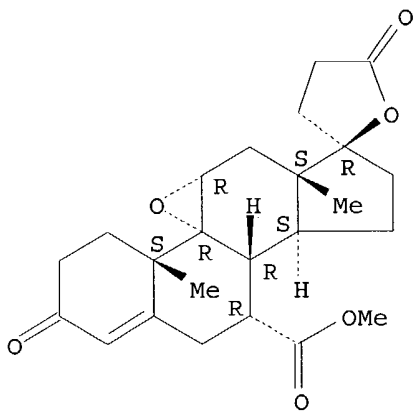
10/608,101

(use of aldosterone antagonist, specifically a spirolactone-type steroidal compound, for treatment or prophylaxis of aldosterone-mediated pathogenic effects)

RN 107724-20-9 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



AB The present invention provides methods for the treatment or prophylaxis of one or more aldosterone-mediated pathogenic effects in a subject suffering from or susceptible to the pathogenic effect or effects wherein the subject has one or more conditions selected from the group consisting of a sub-normal endogenous aldosterone level, salt sensitivity and an elevated dietary sodium intake. The methods comprise administering to the subject a therapeutically-effective amount of one or more aldosterone antagonists, more specifically a spirolactone-type steroidal compound. The compounds can be administered as solvated or non-solvated crystals or in an amorphous form. In addition to use of the compounds, their formulation and crystallization are exemplified.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 25 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:359782 CAPLUS

DOCUMENT NUMBER: 134:361365

TITLE: Methods for treating, inhibiting or preventing pathogenic change resulting from vascular injury with an aldosterone antagonist

INVENTOR(S): Delyani, John A.; Fedde, Kenton N.; Funder, John W.; Ward, Michael R.; Kanellakis, Peter; Bobik, Alex

PATENT ASSIGNEE(S): Pharmacia Corporation, USA

SOURCE: PCT Int. Appl., 57 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

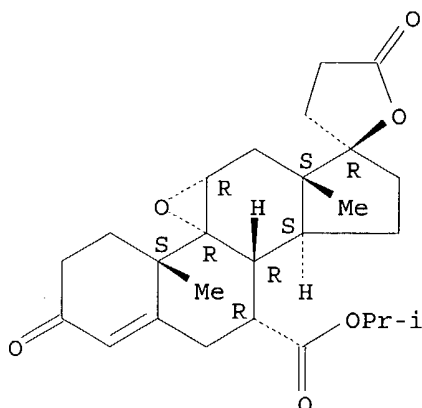
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034132	A2	20010517	WO 2000-US30853	20001108

WO 2001034132 A3 20020124
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1227804 A2 20020807 EP 2000-977121 20001108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2003513913 T2 20030415 JP 2001-536132 20001108
WO 2003051372 A1 20030626 WO 2001-US48419 20011213
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2003191100 A1 20031009 US 2002-243876 20020913
PRIORITY APPLN. INFO.: US 1999-164390P P 19991109
US 2000-211064P P 20000613
US 2000-211250P P 20000613
US 2000-211253P P 20000613
US 2000-211264P P 20000613
US 2000-211311P P 20000613
US 2000-211340P P 20000613
US 2000-211451P P 20000613
US 2000-211459P P 20000613
US 2000-221358P P 20000727
US 2000-221364P P 20000727
US 2000-233056P P 20000914
US 2000-709253 A2 20001108
WO 2000-US30853 W 20001108
US 2000-712543 A1 20001114
IT 95716-76-0 95716-78-2 95716-98-6
95716-99-7 95717-02-5 107724-20-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aldoosterone antagonist for treating, inhibiting or preventing pathogenic change resulting from vascular injury)
RN 95716-76-0 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, 1-methylethyl ester, (7 α ,11 α ,17 α)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

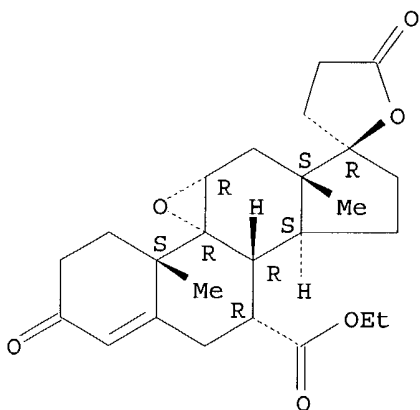
10/608,101



RN 95716-78-2 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, ethyl ester, (7 α ,11 α ,17 α)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry. Rotation (+).

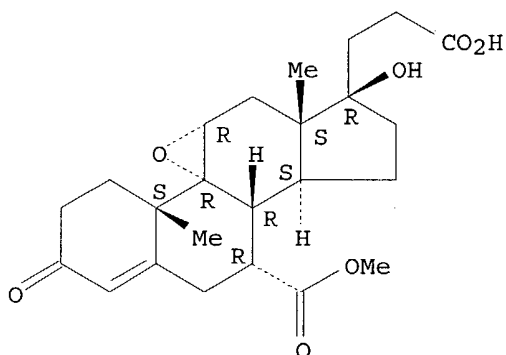


RN 95716-98-6 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-methyl
ester, monopotassium salt, (7 α ,11 α ,17 α)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

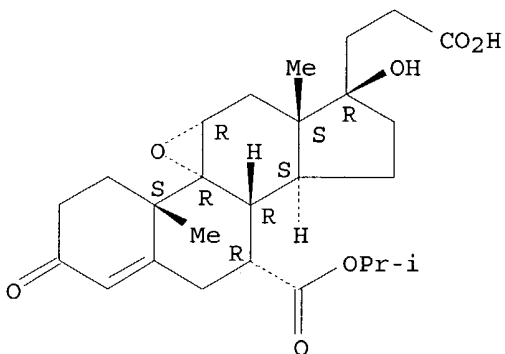
10/608,101



● K

RN 95716-99-7 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
7-(1-methylethyl) ester, monopotassium salt, (7 α ,11 α ,17 α) - (9CI) (CA INDEX NAME)

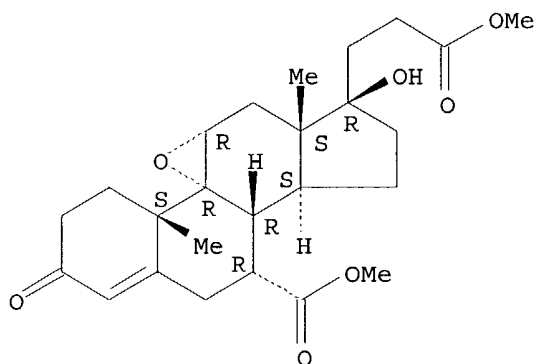
Absolute stereochemistry.



● K

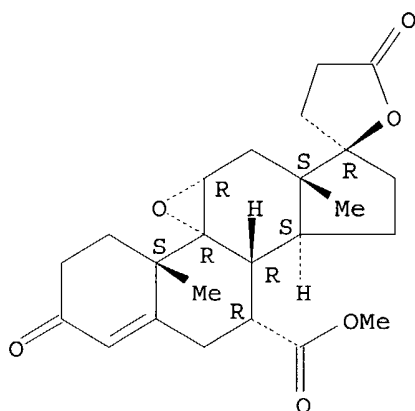
RN 95717-02-5 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, dimethyl
ester, (7 α ,11 α ,17 α) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 107724-20-9 CAPLUS
 CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ-lactone, methyl ester, (7α,11α,17α)- (9CI) (CA
 INDEX NAME)

Absolute stereochemistry.



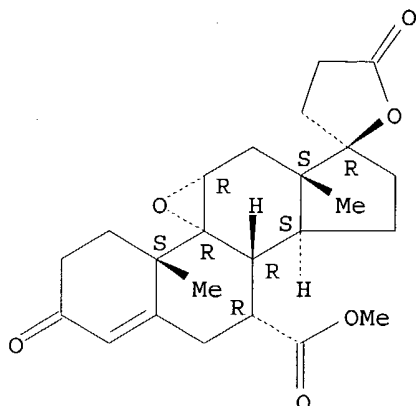
AB Methods are provided for treating, inhibiting or preventing pathogenic change resulting from vascular injury in a subject, particularly restenosis resulting substantially from angioplasty. The methods comprise administering a therapeutically-effective amount of an aldosterone antagonist, particularly eplerenone, in a mammalian subject susceptible to or suffering from the pathogenic change.

L8 ANSWER 26 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2000:628026 CAPLUS
 DOCUMENT NUMBER: 133:227793
 TITLE: Combination therapy of angiotensin converting enzyme inhibitor and epoxy-steroidal aldosterone antagonist for treatment of cardiovascular disease
 INVENTOR(S): Alexander, John C.; Roniker, Barbara; Desai, Subhash
 PATENT ASSIGNEE(S): G.D. Searle and Co., USA
 SOURCE: PCT Int. Appl., 212 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

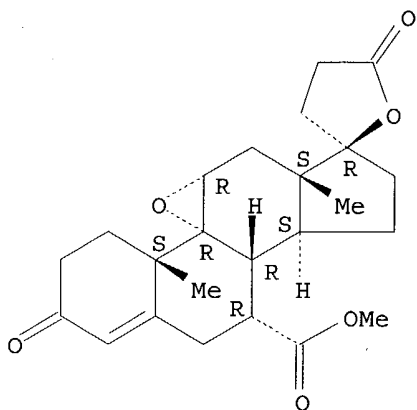
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000051642	A1	20000908	WO 2000-US5633	20000303
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1165136	A1	20020102	EP 2000-912174	20000303
EP 1165136	B1	20030910		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200102581	T2	20020422	TR 2001-200102581	20000303
BR 2000008781	A	20020702	BR 2000-8781	20000303
JP 2002538172	T2	20021112	JP 2000-602308	20000303
AT 249242	E	20030915	AT 2000-912174	20000303
EP 1382351	A1	20040121	EP 2003-19610	20000303
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
ZA 2001007779	A	20021220	ZA 2001-7779	20010920
US 2004077611	A1	20040422	US 2003-440691	20030519
NZ 529635	A	20031219	NZ 2003-529635	20031119
PRIORITY APPLN. INFO.:				
US 1999-122977P P 19990305				
US 1999-122978P P 19990305				
EP 2000-912174 A3 20000303				
US 2000-518854 B1 20000303				
WO 2000-US5633 W 20000303				
IT	107724-20-9, Eplerenone			
	RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)			
	(combination therapy of angiotensin converting enzyme inhibitor and epoxy-steroidal aldosterone antagonist for treatment of cardiovascular disease)			
RN	107724-20-9 CAPLUS			
CN	Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, methyl ester, (7 α ,11 α ,17 α)-(9CI) (CA INDEX NAME)			

Absolute stereochemistry.



IT 107724-20-9DP, Eplerenone, derivs.
 RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); USES (Uses)
 (combination therapy of angiotensin converting enzyme inhibitor and
 epoxy-steroidal aldosterone antagonist for treatment of cardiovascular
 disease)
 RN 107724-20-9 CAPLUS
 CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ-lactone, methyl ester, (7α,11α,17α)- (9CI) (CA
 INDEX NAME)

Absolute stereochemistry.



AB Combinations of an ACE inhibitor and an epoxy-steroidal aldosterone
 receptor antagonist are described for use in treatment of circulatory
 disorders. Of particular interest are therapies using
 epoxy-steroidal-type aldosterone receptor antagonist compds., such as
 eplerenone, in combination with an angiotensin converting enzyme
 inhibitor. This co-therapy would be particularly useful to treat
 congestive heart failure while avoiding or reducing aldosterone-antagonist-
 induced side effects such as hyperkalemia. Capsules were prepared containing
 captopril 62.0 and eplerenone 12.5 mg/capsule.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 27 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 1998:405970 CAPLUS

DOCUMENT NUMBER: 129:81885

TITLE: Processes for preparation of 9,11-

epoxy steroids and their
intermediatesINVENTOR(S): Ng, John S.; Liu, Chin; Anderson, Dennis K.; Lawson,
Jon P.; Wieczorek, Joseph; Kunda, Sastry A.; Letendre,
Leo J.; Pozzo, Mark J.; Sing, Yuen-lung L.; Wang, Ping
T.; Yonan, Edward E.; Weier, Richard M.; Kowar, Thomas
R.; Baez, Julio A.; Erb, BernhardPATENT ASSIGNEE(S): G.D. Searle and Co., USA; Ng, John S.; Liu, Chin;
Anderson, Dennis K.; Lawson, Jon P.; Wieczorek,
Joseph; Kunda, Sastry A.; Letendre, Leo J.; Pozzo,
Mark J.; et al.

SOURCE: PCT Int. Appl., 543 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9825948	A2	19980618	WO 1997-US23090	19971211
WO 9825948	A3	19981015		
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
ZA 9711038	A	19990125	ZA 1997-11038	19971209
AU 9857983	A1	19980703	AU 1998-57983	19971211
AU 733559	B2	20010517		
EP 944644	A2	19990929	EP 1997-954126	19971211
EP 944644	B1	20021002		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI			
CN 1253564	A	20000517	CN 1997-181737	19971211
BR 9714510	A	20001128	BR 1997-14510	19971211
NZ 336004	A	20010427	NZ 1997-336004	19971211
JP 2001509792	T2	20010724	JP 1998-527032	19971211
EP 1148061	A2	20011024	EP 2001-111209	19971211
EP 1148061	A3	20040728		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI			
EP 1223174	A2	20020717	EP 2002-7309	19971211
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI			
AT 225367	E	20021015	AT 1997-954126	19971211
NZ 510556	A	20021025	NZ 1997-510556	19971211
ES 2186017	T3	20030501	ES 1997-954126	19971211
ZA 9805088	A	19990611	ZA 1998-5088	19980611
NO 9902825	A	19990729	NO 1999-2825	19990610
AU 747959	B2	20020530	AU 2000-18440	20000221
US 2002038021	A1	20020328	US 2000-732208	20001207
US 2002045746	A1	20020418	US 2000-732209	20001207
US 2003055274	A1	20030320	US 2002-112355	20020329
US 6610844	B2	20030826		
PRIORITY APPLN. INFO.:			US 1996-33315P	P 19961211

US 1997-49388P	P 19970611
US 1995-8455P	P 19951211
US 1996-763910	A3 19961211
EP 1997-954126	A3 19971211
NZ 1997-336004	A1 19971211
WO 1997-US23090	W 19971211
US 1999-246204	A2 19990208
US 1999-246908	A3 19990209
US 1999-169556P	P 19991208
US 1999-169608P	P 19991208
US 1999-169639P	P 19991208
US 1999-169682P	P 19991208
US 1999-169683P	P 19991208
US 1999-169690P	P 19991208
US 1999-169707P	P 19991208
US 1999-169807P	P 19991208
US 1999-319673	A2 19991213
US 2000-583137	A2 20000530
US 2000-583158	A2 20000530

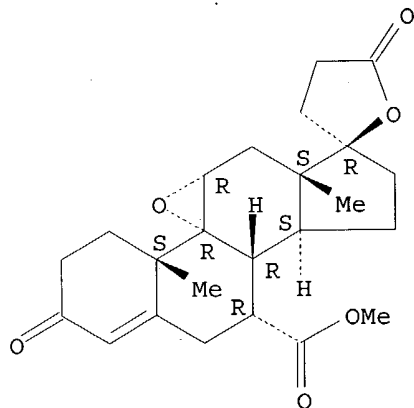
OTHER SOURCE(S): CASREACT 129:81885; MARPAT 129:81885

IT 107724-20-9P 209253-80-5P 209253-81-6P
209253-82-7PRL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP
(Preparation)(processes for preparation of 9,11-epoxy
steroids and their intermediates)

RN 107724-20-9 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



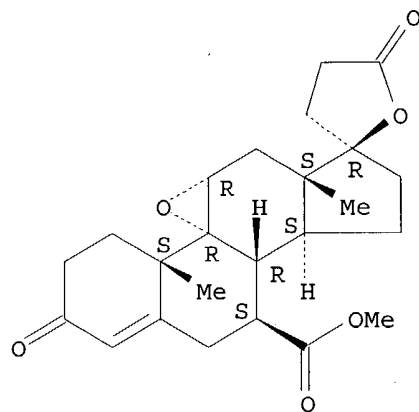
RN 209253-80-5 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-6,17-dihydroxy-3-oxo-,
 γ -lactone, methyl ester, (6 β ,7 α ,11 α ,17 α)-
(9CI) (CA INDEX NAME)

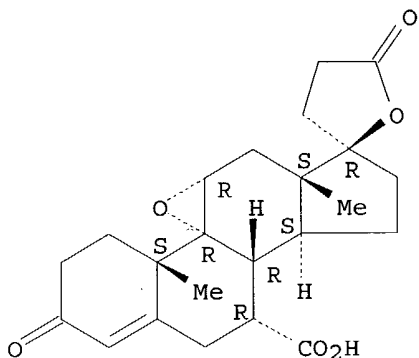
Absolute stereochemistry.

Chemical structure 1: A complex steroid derivative. The structure shows a steroid nucleus with several functional groups and stereocenters. Key features include a ketone at C-3, a double bond at C-4, a methyl group at C-10, a hydroxyl group at C-13, a methoxycarbonyl group at C-14, and a complex side chain at C-17 that includes a ketone, a methyl group, and a cyclic ether.

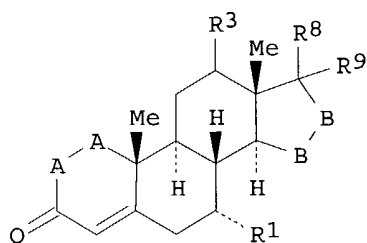
Absolute stereochemistry.



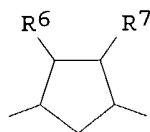
Absolute stereochemistry.



GI



I



II

AB Multiple novel reaction schemes, novel process steps and novel intermediates are provided for the synthesis of epoxymexrenone and other compds. of formula (I) wherein: -A-A- represents the group -CHR4-CHR5- or -CR4=CR5-, R3, R4 and R5 are independently selected from the group consisting of hydrogen, halo, hydroxy, lower alkyl, lower alkoxy, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, cyano, aryloxy; R1 represents an alpha-oriented lower alkoxycarbonyl or hydroxyalkyl radical; -B-B- represents the group -CHR6-CHR7- or an alpha- or beta-oriented group (II), where R6 and R7 are independently selected from the group consisting of hydrogen, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, alkoxycarbonyl, acyloxyalkyl, cyano and aryloxy; and R8 and R9 are independently selected from the group consisting of hydrogen, hydroxy, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, alkoxycarbonyl, acyloxyalkyl, cyano and aryloxy, or R8 and R9 together comprise a carbocyclic or heterocyclic ring structure, or R8 or R9 together with R6 or R7 comprise a carbocyclic or heterocyclic ring structure fused to the pentacyclic D ring.

L8 ANSWER 28 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 4

ACCESSION NUMBER: 1997:511895 CAPLUS

DOCUMENT NUMBER: 127:120750

TITLE: Preparation of 7 α -carboxyl- 9,

11-epoxy steroids and

intermediates useful therein and a general process for the epoxidation of olefinic double bonds

INVENTOR(S):

Ng, John S.; Wang, Ping T.; Baez, Julio A.; Liu, Chin; Anderson, Dennis K.; Lawson, Jon P.; Erb, Dernhard;

Wieczorek, Joseph; Mucciariello, Gennaro; Vanzanella,
Fortunato; Kunda, Sastry A.; Letendre, Leo J.; Pozzo,
Mark J.; Sing, Yuen-Lung L.

PATENT ASSIGNEE(S):

G.D. Searle and Co., USA

SOURCE:

PCT Int. Appl., 271 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

6

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9721720	A2	19970619	WO 1996-US20780	19961211
W:			AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM	
RW:			KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG	
CA 2240388	AA	19970619	CA 1996-2240388	19961211
CA 2347345	AA	19970619	CA 1996-2347345	19961211
CA 2347346	AA	19970619	CA 1996-2347346	19961211
AU 9713551	A1	19970703	AU 1997-13551	19961211
AU 719260	B2	20000504		
CN 1209136	A	19990224	CN 1996-199961	19961211
US 5981744	A	19991109	US 1996-763910	19961211
EP 973791	A2	20000126	EP 1996-945103	19961211
R:			AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI	
EP 1167380	A2	20020102	EP 2001-122428	19961211
R:			AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI	
EP 1167381	A2	20020102	EP 2001-122429	19961211
R:			AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI	
EP 1170299	A2	20020109	EP 2001-122427	19961211
R:			AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI	
JP 2002504077	T2	20020205	JP 1997-522304	19961211
AU 744223	B2	20020221	AU 2000-18439	20000221
US 2004067917	A1	20040408	US 2003-672680	20030926
PRIORITY APPLN. INFO.:			US 1995-8455P	P 19951211
			US 1996-763910	A 19961211
			EP 1996-945103	A3 19961211
			WO 1996-US20780	W 19961211
			US 1999-246908	A3 19990209
			US 2000-583158	A3 20000530
			US 2001-923977	A3 20010807

OTHER SOURCE(S):

CASREACT 127:120750; MARPAT 127:120750

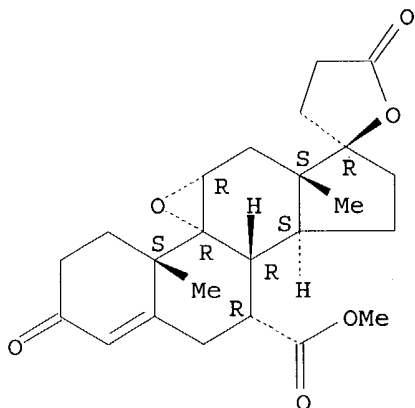
IT 107724-20-9P

RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of 7 α -carboxyl- 9,11-epoxy
steroids and intermediates useful therein and a general process
for the epoxidn. of olefinic double bonds)

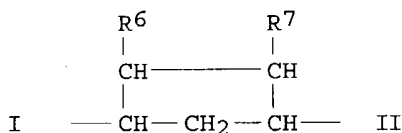
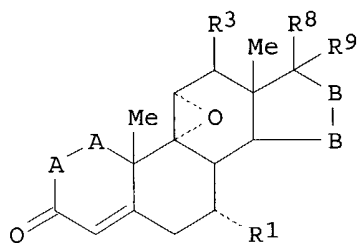
RN 107724-20-9 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



GI



AB Multiple novel reaction schemes, novel process steps and novel intermediates are provided for the synthesis of epoxymexrenone and other compds. of formula (I), wherein -A-A- represents the group -CHR⁴-CHR⁵- or -CR⁴=CR⁵-; R³, R⁴ and R⁵ are independently selected from the group consisting of H, halo, OH, lower alkyl, lower alkoxy, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, CN, aryloxy; R¹ represents an α -oriented lower alkoxyalkyl or hydroxyalkyl radical; -B-B- represents the group -CHR⁶-CHR⁷- or an α - or β -oriented group of formula (II) where R⁶ and R⁷ are independently selected from the group consisting of H, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, alkoxyalkyl, acyloxyalkyl, CN, aryloxy, and R⁸ and R⁹ are independently selected from the group consisting of H, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, alkoxyalkyl, acyloxyalkyl, CN, aryloxy, or R⁸ and R⁹ together comprise a carbocyclic or heterocyclic ring structure, or R⁸ or R⁹ together with R⁶ or R⁷ comprise a carbocyclic or heterocyclic ring structure fused to the pentacyclic D ring.

L8 ANSWER 29 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:240285 CAPLUS

DOCUMENT NUMBER: 126:277650

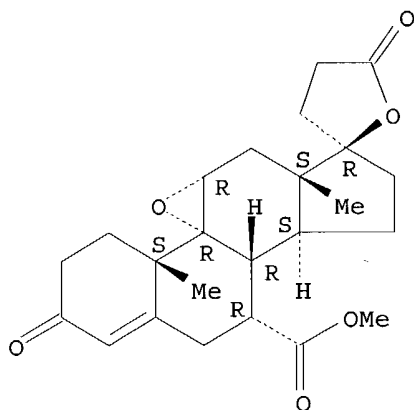
TITLE: Steroidal, aldosterone antagonists. Increased selectivity of 9 α ,11-epoxy derivatives

AUTHOR(S): Grob, Jurgen; Boillaz, Michel; Schmidlin, Julius; Wehrli, Hansuli; Wieland, Peter; Fuhrer, Hermann;

10/608,101

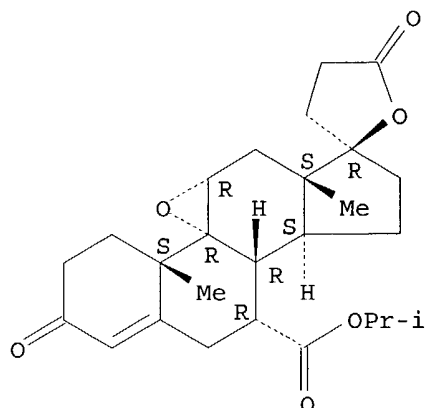
Rihs, Greta; Joss, Urs; De Gasparo, Marc; et al.
CORPORATE SOURCE: Research Dep., Ciba-Geigy Ltd., Basel, CH-4002, Switz.
SOURCE: Helvetica Chimica Acta (1997), 80(2), 566-585
CODEN: HCACAV; ISSN: 0018-019X
PUBLISHER: Verlag Helvetica Chimica Acta
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 107724-20-9P, CGP 30083
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and aldosterone antagonistic activity of epoxy pregnanes)
RN 107724-20-9 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, methyl ester, (7 α ,11 α ,17 α)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



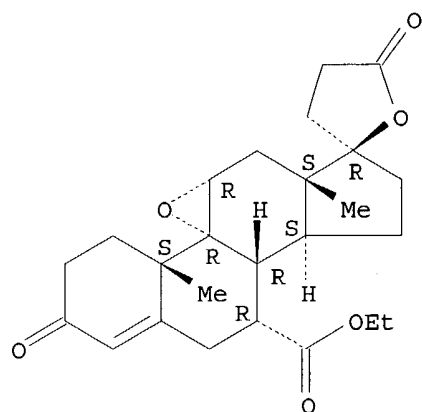
IT 95716-76-0P 95716-78-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and aldosterone antagonistic activity of epoxy pregnanes)
RN 95716-76-0 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ -lactone, 1-methylethyl ester, (7 α ,11 α ,17 α)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 95716-78-2 CAPLUS
 CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ-lactone, ethyl ester, (7α,11α,17α)- (9CI) (CA
 INDEX NAME)

Absolute stereochemistry. Rotation (+).



AB In the search for aldosterone antagonists with an optimal activity profile, 12 9α,11-epoxy **steroids** were prepared and compared with their 9α,11α-unsubstituted analogs in terms of steroid receptor binding in vitro and electrolyte excretion in vivo. Substitution of the parent structures by an epoxy group at positions 9α,11 resulted in marginal effects on mineralocorticoid receptor binding and electrolyte excretion, but greatly reduced androgen and gestagen receptor binding. This finding is reflected in the largely lacking unwanted anti-androgenic and gestagenic side effects in animal models of the 3 most interesting 9α,11-epoxy spiro lactones CGP 33033, CGP 29245, and CGP 30083.

L8 ANSWER 30 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1997:168547 CAPLUS
 DOCUMENT NUMBER: 126:152803
 TITLE: Epoxy-steroidal aldosterone antagonist and angiotensin II antagonist combination therapy for treatment of cardiovascular disorders, including congestive heart

10/608,101

failure
INVENTOR(S): Alexander, John C.; Schuh, Joseph R.; Gorczynski, Richard J.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA; Alexander, John C.; Schuh, Joseph R.; Gorczynski, Richard J.
SOURCE: PCT Int. Appl., 218 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9640257	A1	19961219	WO 1996-US9335	19960605
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
CA 2224079	AA	19961219	CA 1996-2224079	19960605
AU 9661577	A1	19961230	AU 1996-61577	19960605
AU 725689	B2	20001019		
EP 831910	A1	19980401	EP 1996-919170	19960605
EP 831910	B1	20011121		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
CN 1192697	A	19980909	CN 1996-196155	19960605
BR 9609066	A	19990126	BR 1996-9066	19960605
JP 11507627	T2	19990706	JP 1996-501678	19960605
NZ 310730	A	20010126	NZ 1996-310730	19960605
RU 2166330	C2	20010510	RU 1998-100250	19960605
IL 122242	A1	20010724	IL 1996-122242	19960605
AT 209047	E	20011215	AT 1996-919170	19960605
ES 2167571	T3	20020516	ES 1996-919170	19960605
PT 831910	T	20020531	PT 1996-919170	19960605
RO 118046	B1	20030130	RO 1997-2272	19960605
PL 185150	B1	20030331	PL 1996-324001	19960605
US 6653306	B1	20031125	US 1997-781786	19970109
NO 9705741	A	19980129	NO 1997-5741	19971205
PRIORITY APPLN. INFO.:			US 1995-486456	A 19950607
			WO 1996-US9335	W 19960605

OTHER SOURCE(S): MARPAT 126:152803

IT 95716-76-0 95716-78-2 95716-98-6

95716-99-7 95717-02-5 107724-20-9

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

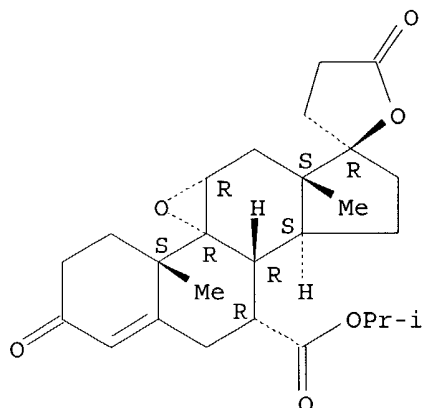
(epoxy-steroidal aldosterone antagonist and angiotensin II antagonist combination therapy for treatment of cardiovascular disorders, including congestive heart failure)

RN 95716-76-0 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, 1-methylethyl ester, (7 α ,11 α ,17 α)-(9CI) (CA INDEX NAME)

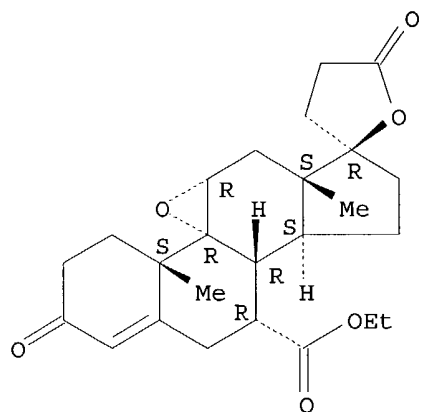
Absolute stereochemistry. Rotation (-).

10/608,101



RN 95716-78-2 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, ethyl ester, (7α,11α,17α)- (9CI) (CA
INDEX NAME)

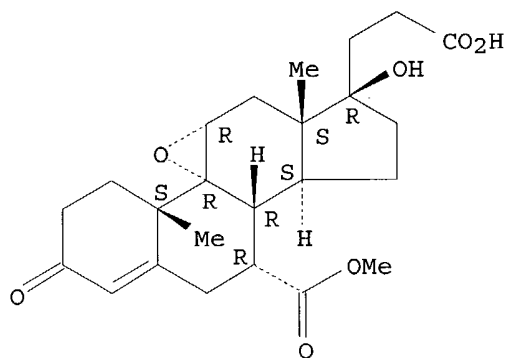
Absolute stereochemistry. Rotation (+).



RN 95716-98-6 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-methyl
ester, monopotassium salt, (7α,11α,17α)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

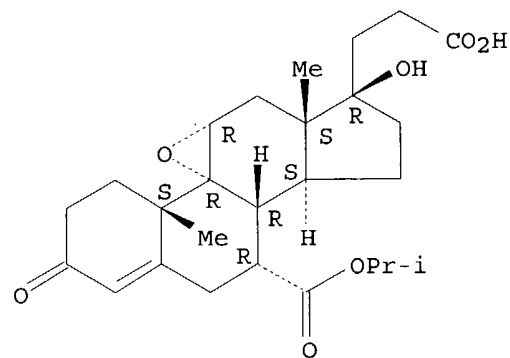
10/608,101



● K

RN 95716-99-7 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
7-(1-methylethyl) ester, monopotassium salt, (7 α ,11 α ,17 α) - (9CI) (CA INDEX NAME)

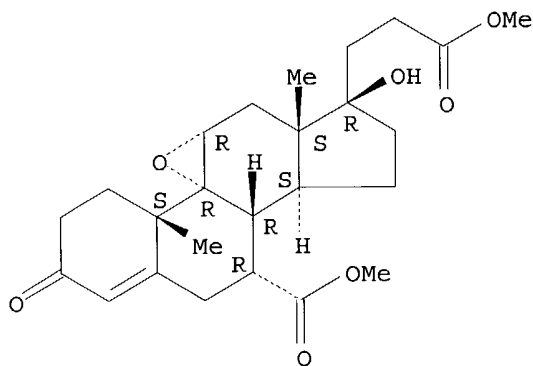
Absolute stereochemistry.



● K

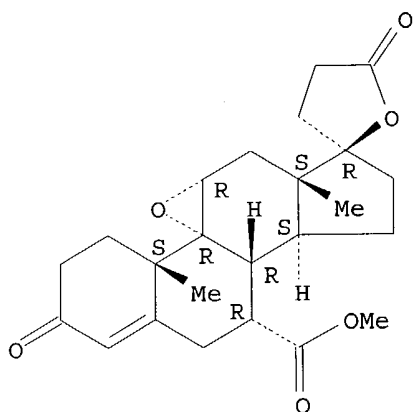
RN 95717-02-5 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, dimethyl
ester, (7 α ,11 α ,17 α) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 107724-20-9 CAPLUS
 CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ-lactone, methyl ester, (7α,11α,17α)- (9CI) (CA
 INDEX NAME)

Absolute stereochemistry.



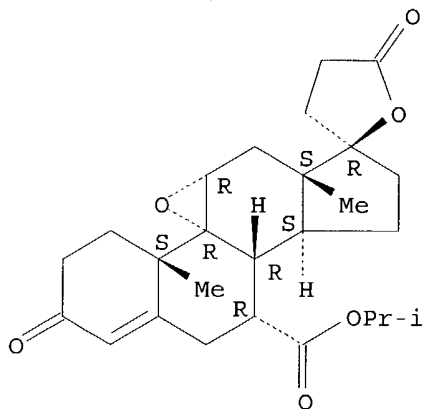
AB A combination therapy comprising a therapeutically-effective amount of an epoxy-steroidal aldosterone receptor antagonist and a therapeutically-effective amount of an angiotensin II receptor antagonist is described for treatment of circulatory disorders, including cardiovascular disorders, e.g. hypertension and congestive heart failure. Preferred angiotensin II receptor antagonists are those compds. having high potency and bioavailability and which are characterized in having an imidazole or triazole moiety attached to a biphenylmethyl or pyridinyl/phenylmethyl moiety. Preferred epoxy-steroidal aldosterone receptor antagonists are 20-spiroxane steroidal compds. characterized by the presence of 9α,11α-substituted epoxy moiety. A preferred combination therapy includes the angiotensin II receptor antagonist 5-[2-[5-[(3,5-dibutyl-1H-1,2,4-triazol-1-yl)methyl]-2-pyridinyl]phenyl]-1H-tetrazole and the aldosterone receptor antagonist epoxymexrenone.

L8 ANSWER 31 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1997:140243 CAPLUS
 DOCUMENT NUMBER: 126:139886
 TITLE: Method to treat cardiofibrosis or cardiac hypertrophy
 with a combination therapy of an angiotensin II

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9640255	A2	19961219	WO 1996-US8709	19960605
WO 9640255	A3	19970123		
W:	AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG			
RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA			
AU 9660392	A1	19961230	AU 1996-60392	19960605
PRIORITY APPLN. INFO.:			US 1995-486085	19950607
			WO 1996-US8709	19960605

IT	95716-76-0 95716-78-2 95716-98-6 95716-99-7 95717-02-5 107724-20-9 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (angiotensin II antagonist and epoxy-steroidal aldosterone antagonist combination for treatment of cardiofibrosis or cardiac hypertrophy)
RN	95716-76-0 CAPLUS
CN	Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ-lactone, 1-methylethyl ester, (7α,11α,17α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

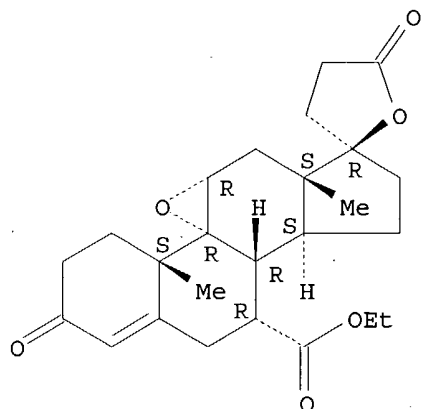


RN	95716-78-2	CAPLUS
CN	Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, ethyl ester, (7 α ,11 α ,17 α)- (9CI) (CA	

10/608,101

INDEX NAME)

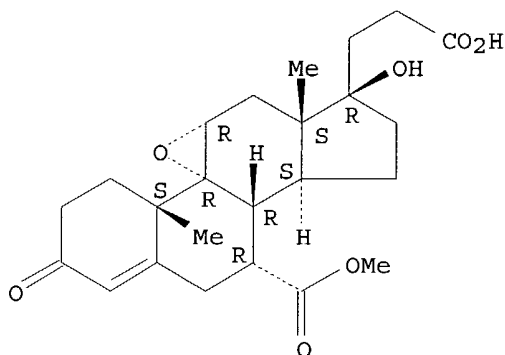
Absolute stereochemistry. Rotation (+).



RN 95716-98-6 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-methyl ester, monopotassium salt, (7 α ,11 α ,17 α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



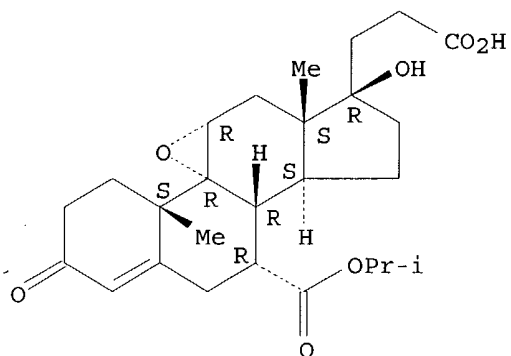
● K

RN 95716-99-7 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-(1-methylethyl) ester, monopotassium salt, (7 α ,11 α ,17 α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10/608,101

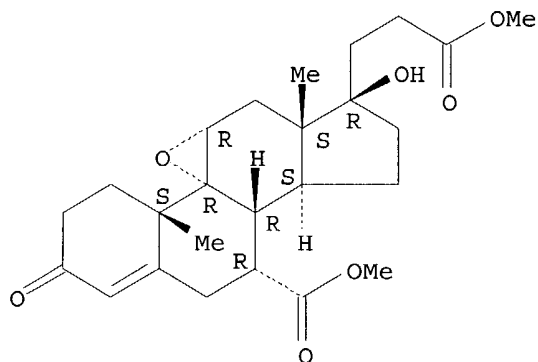


● K

RN 95717-02-5 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, dimethyl ester, (7 α ,11 α ,17 α)- (9CI) (CA INDEX NAME)

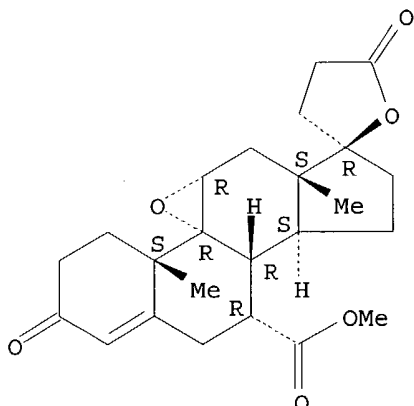
Absolute stereochemistry.



RN 107724-20-9 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
 γ-lactone, methyl ester, (7α,11α,17α)- (9CI) (CA
 INDEX NAME)

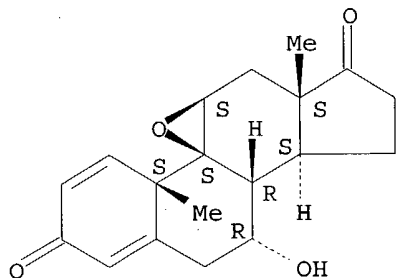
Absolute stereochemistry.



AB A therapeutic method is described for treating cardiofibrosis or cardiac hypertrophy using a combination therapy comprising a therapeutically effective amount of an epoxy-steroidal aldosterone receptor antagonist and a therapeutically-effective amount of an angiotensin II receptor antagonist. Preferred angiotensin II receptor antagonists are those compds. having high potency and bioavailability and which are characterized in having an imidazole or triazole moiety attached to a biphenylmethyl or pyridinyl/phenylmethyl moiety. Preferred epoxy-steroidal aldosterone receptor antagonists are 20-spiroxane steroidal compds. characterized by the presence of a 9 α ,11 α -substituted epoxy moiety. A preferred combination therapy includes the angiotensin II receptor antagonist 5-[2-[5-[(3,5-dibutyl-1H-1,2,4-triazol-1-yl)methyl]-2-pyridinyl]phenyl]-1H-tetrazole and the aldosterone receptor antagonist epoxymexrenone.

L8 ANSWER 32 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1995:14188 CAPLUS
 DOCUMENT NUMBER: 122:240124
 TITLE: Investigations into the alkaline instability of 7 α -hydroxy metabolites of tipredane
 AUTHOR(S): Crew, Jacqueline; Euerby, Melvin R.; Johnson, Christopher M.; Morlin, Andrew J. G.; Thomson, Colin
 CORPORATE SOURCE: Res. Dev. Lab., Fisons Pharm., Leicestershire, LE11 0RH, UK
 SOURCE: Analytical Proceedings (1994), 31(4), 127-30
 CODEN: ANPRDI; ISSN: 0144-557X
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 IT 162125-01-1P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (alkaline degradation of 7 α -hydroxy metabolites of tipredane)
 RN 162125-01-1 CAPLUS
 CN Androsta-1,4-diene-3,17-dione, 9,11-epoxy-7-hydroxy-, (7 α ,9 β ,11 β)- (9CI) (CA INDEX NAME)

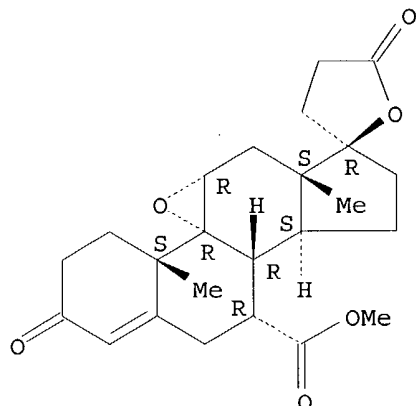
Absolute stereochemistry.



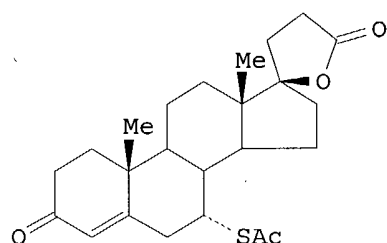
AB The reaction of the rodent metabolites of tipredane with sodium hydroxide has been investigated. The major degradant has been characterized as a 9,11 β -epoxide and represents the first reported case of the elimination of hydrogen fluoride from 9 α -fluoro-11 β -hydroxy substituted **steroids**. The 7 α -hydroxy moiety in these metabolites has been shown to promote the hydrogen fluoride elimination reaction in the presence of sodium hydroxide. The rate of hydrogen fluoride elimination vs. dehydration of the 7 α -hydroxy substituent is influenced by the sodium hydroxide concentration and the solvent composition

L8 ANSWER 33 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1989:128777 CAPLUS
 DOCUMENT NUMBER: 110:128777
 TITLE: Antialdosterones: incidence and prevention of sexual side effects
 AUTHOR(S): De Gasparo, M.; Whitebread, S. E.; Preiswerk, G.; Jeunemaitre, X.; Corvol, P.; Menard, J.
 CORPORATE SOURCE: Pharm. Div., CIBA-GEIGY Ltd., Basel, Switz.
 SOURCE: Journal of Steroid Biochemistry (1989), 32(1B), 223-7
 CODEN: JSTBBK; ISSN: 0022-4731
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 IT 107724-20-9
 RL: BIOL (Biological study)
 (as antialdosterone antihypertensive, potassium and sodium of urine response to, in human)
 RN 107724-20-9 CAPLUS
 CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, methyl ester, (7 α ,11 α ,17 α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



I

AB The use of spironolactone in the treatment of hypertension has been limited by the occurrence of sexual effects, mainly menstrual disturbances in women and gynecomastia in men. To minimize this limitation on the use of an effective K-sparing antihypertensive agent, 2 strategies were proposed: a decrease in the daily dose of spironolactone and improvement in the receptor-binding specificity of spironolactone. In 182 patients with essential hypertension treated with spironolactone alone for a mean follow-up period of 23 mo, daily doses of 75-100 mg were as effective on blood pressure as doses of 150-300 mg. In contrast, the development of gynecomastia (91 cases among 699 men) was dose-related in 6.9% (50 mg/day) to 52.2% (≥ 150 mg/day) of the cases. Two $9\alpha,11\alpha$ -epoxy derivs. were characterized in vitro in rats and in rabbits. They exhibited a 3-10-fold decrease of the antiandrogenic and progestagenic effect, compared with spironolactone. In humans, 1 of these derivs., epoxymexrenone (I) counteracted the fall in urinary Na/K ratio induced by 9α -fluorohydrocortisone at a 25 mg dose.

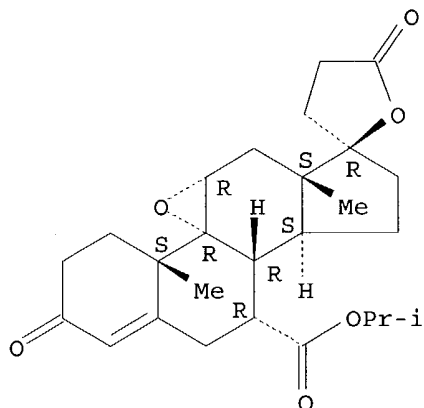
L8 ANSWER 34 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1985:149622 CAPLUS
 DOCUMENT NUMBER: 102:149622
 TITLE: 20-Spiroxanes and analogs with open ring E
 INVENTOR(S): Grob, Juergen; Kalvoda, Jaroslav
 PATENT ASSIGNEE(S): Ciba-Geigy A.-G., Switz.
 SOURCE: Eur. Pat. Appl., 57 pp.
 CODEN: EPXXDW

10/608,101

DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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EP 122232	A1	19841017	EP 1984-810179	19840410
EP 122232	B1	19881214		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
FI 8401400	A	19841014	FI 1984-1400	19840409
FI 77669	B	19881230		
FI 77669	C	19890410		
→US 4559332	A	19851217	US 1984-598109	19840409
AT 39256	E	19881215	AT 1984-810179	19840410
ES 531517	A1	19851201	ES 1984-531517	19840411
DD 233375	A5	19860226	DD 1984-276211	19840411
CA 1220781	A1	19870421	CA 1984-451691	19840411
IL 71504	A1	19870731	IL 1984-71504	19840411
DD 251144	A5	19871104	DD 1984-261867	19840411
DK 8401894	A	19841014	DK 1984-1894	19840412
DK 163988	B	19920427		
DK 163988	C	19920921		
NO 8401465	A	19841015	NO 1984-1465	19840412
NO 159800	B	19881031		
NO 159800	C	19890208		
AU 8426853	A1	19841018	AU 1984-26853	19840412
AU 565017	B2	19870903		
ZA 8402710	A	19841128	ZA 1984-2710	19840412
JP 59231100	A2	19841225	JP 1984-71900	19840412
JP 02012479	B4	19900320		
HU 33814	O	19841228	HU 1984-1435	19840412
HU 191406	B	19870227		
ES 544768	A1	19870501	ES 1985-544768	19850701
ES 544769	A1	19870501	ES 1985-544769	19850701
ES 544770	A1	19870501	ES 1985-544770	19850701
PRIORITY APPLN. INFO.:			CH 1983-1981	19830413
			EP 1984-810179	19840410
IT 95716-76-0P				
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT				
(Reactant or reagent)				
(preparation and saponification of)				
RN 95716-76-0 CAPLUS				
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,				
γ -lactone, 1-methylethyl ester, (7 α ,11 α ,17 α)-				
(9CI) (CA INDEX NAME)				

Absolute stereochemistry. Rotation (-).



IT 95716-78-2P 95716-98-6P 95716-99-7P

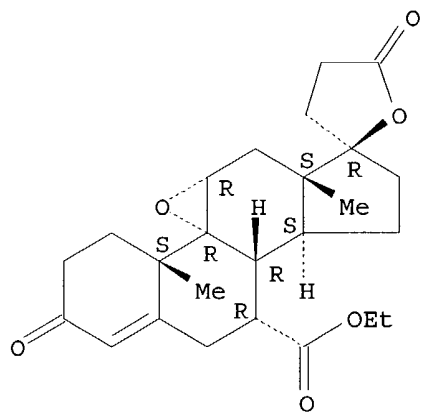
95717-02-5P 107724-20-9P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 95716-78-2 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, ethyl ester, (7α,11α,17α)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry. Rotation (+).

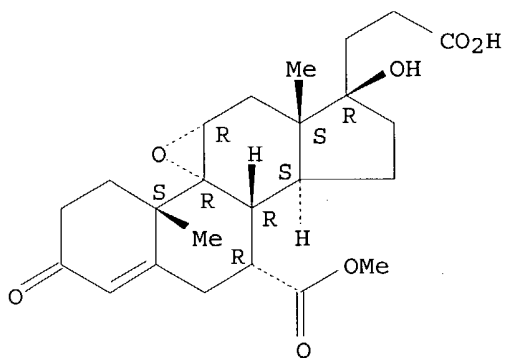


RN 95716-98-6 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-methyl
ester, monopotassium salt, (7α,11α,17α)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

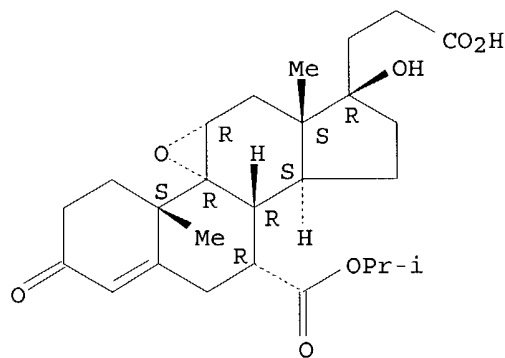
10/608,101



● K

RN 95716-99-7 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
7-(1-methylethyl) ester, monopotassium salt, (7 α ,11 α ,17 α) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

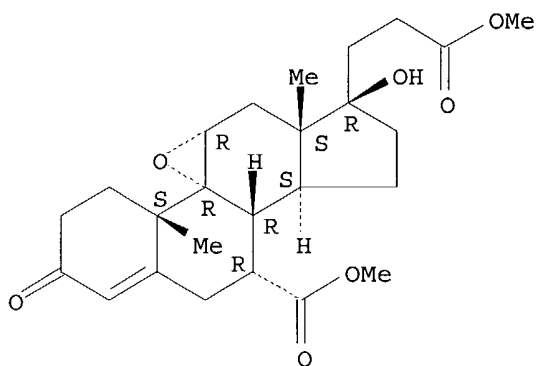


● K

RN 95717-02-5 CAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, dimethyl
ester, (7 α ,11 α ,17 α) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

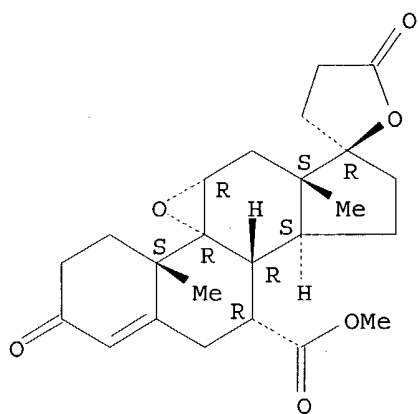
10/608,101



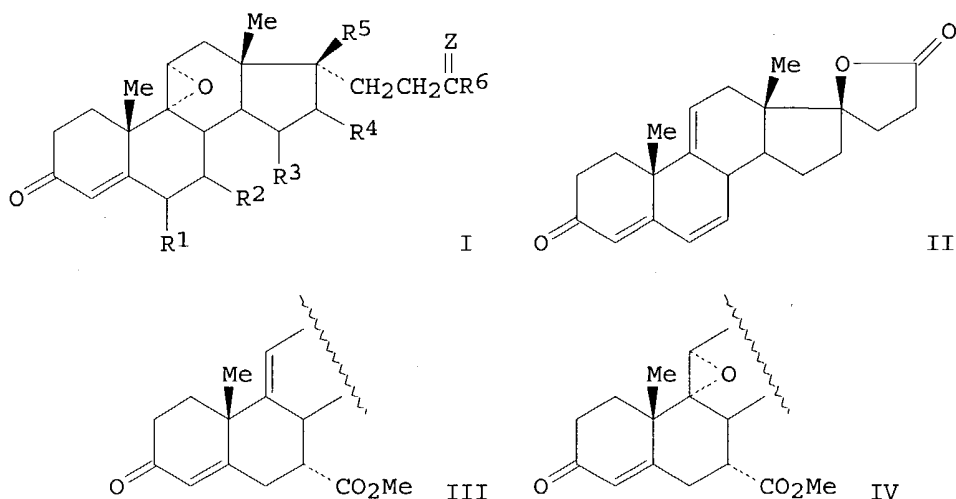
RN 107724-20-9 CAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,
γ-lactone, methyl ester, (7α,11α,17α)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



GI



AB Aldosterone antagonists (no data) I [R1 = H, R2 = α -alkoxycarbonyl, R1R2 = CH2; R3 = R4 = H, R3R4 = CH2; Z = H2, O; R5R6 = O; R5 = HO; R6 = HO, alkoxy, acyloxy; C(Z)R6 = CO2H salts; optionally 1-unsatd.] were prepared from spiroxenones. Thus, spiroxatrienedione II underwent successive hydrocyanation, reduction-hydrolysis, oxidation, and esterification to give acid ester III, which was epoxidized by 3-ClC6H4C(O)O2H to give IV.

L8 ANSWER 35 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1972:127273 CAPLUS

DOCUMENT NUMBER: 76:127273

TITLE: Pharmacologically active 6-azidopregn-4-ene-3,20-diones

INVENTOR(S): Teutsch, Jean G.; Rausser, Richard C.; Shapiro, Elliot L.; Herzog, Hershel L.

PATENT ASSIGNEE(S): Scherico Ltd.

SOURCE: Ger. Offen., 197 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2136655	A	19720127	DE 1971-2136655	19710722
US 3665017	A	19720523	US 1970-58162	19700724
CH 596235	A	19780315	CH 1971-10709	19710720
ZA 7104895	A	19720927	ZA 1971-4895	19710722
DD 94811	C	19730112	DD 1971-156667	19710722
AU 7131568	A1	19730125	AU 1971-31568	19710722
AT 307641	B	19730525	AT 1971-6374	19710722
DK 130150	B	19741230	DK 1971-3612	19710722
SE 384215	B	19760426	SE 1971-9443	19710722
NO 136577	B	19770620	NO 1971-2790	19710722
BE 770378	A1	19720124	BE 1971-106246	19710723
NL 7110181	A	19720126	NL 1971-10181	19710723
FR 2100952	A1	19720324	FR 1971-27054	19710723

10/608,101

FR 2100952	A5	19720324		
GB 1352267	A	19740508	GB 1971-34587	19710723
FI 50129	B	19750901	FI 1971-2102	19710723
CA 983016	A1	19760203	CA 1971-119008	19710723
US 3784603	A	19740108	US 1972-271463	19720713
DK 135132	B	19770307	DK 1973-3195	19730608
CA 983017	A2	19760203	CA 1974-197885	19740419
CA 992951	A2	19760713	CA 1974-197884	19740419
PRIORITY APPLN. INFO.:			US 1970-58162	19700724
			US 1970-59367	19700729
			DK 1971-3612	19710722
			CA 1971-119008	19710723

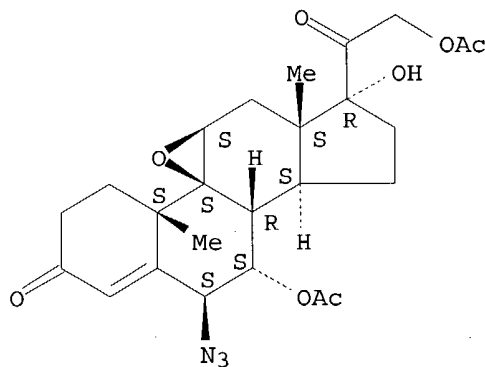
IT 35862-83-0P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 35862-83-0 CAPLUS

CN Pregn-4-ene-3,20-dione, 7,21-bis(acetyloxy)-6-azido-9,11-epoxy-17-hydroxy-
, (6 β ,7 α ,9 β ,11 β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI For diagram(s), see printed CA Issue.

AB The 6-azido-4,6-pregnadiene-3,20-diones I (R = H, OH, Cl, F; R1 = H, Ac; R2 = H, α -Me, β -Me; X = H, F) and some related 11-oxo-compds., 7 α -acetoxy-4-pregnenes, 7 α -acetoxy-4,9(11)-pregnadienes, and 1,4-pregnadienes were prepared. They had antiinflammatory and mineralocorticoid activity. In the systemic pouch test II was .apprx.15 times as active as 6-dehydrocortisone 21-acetate. I (R = OH, R1 = Ac, R2 = H, X = H) was prepared by epoxidizing 11 β ,17 α ,-21-trihydroxy-4,6-pregnadiene-3,20-dione 21 acetate, treating the epoxide with NaN₃, acetylating the 7 α -hydroxy group, and oxidizing with Me₄NF.

L8 ANSWER 36 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 5

ACCESSION NUMBER: 1968:3127 CAPLUS

DOCUMENT NUMBER: 68:3127

TITLE: 7-Methyltestosterones

INVENTOR(S): Babcock, John C.; Campbell, J. Allan

PATENT ASSIGNEE(S): Upjohn Co., USA

SOURCE: U.S., 18 pp.

CODEN: USXXAM

DOCUMENT TYPE: Patent

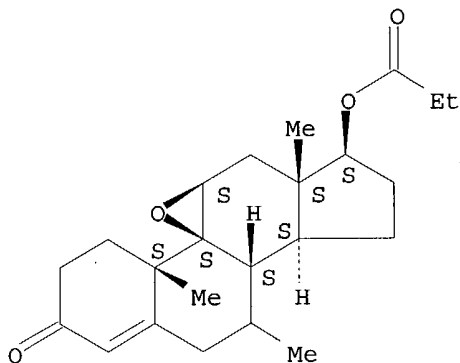
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

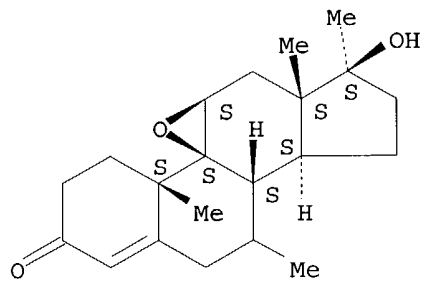
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
	US 334155		19670912	US	19610605
IT	17000-70-3P 17000-71-4P				
	RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of)				
RN	17000-70-3 CAPLUS				
CN	9 β -Androst-4-en-3-one, 9,11 β -epoxy-17 β -hydroxy-7-methyl-, propionate (6CI, 8CI) (CA INDEX NAME)				

Absolute stereochemistry.



RN 17000-71-4 CAPLUS
 CN 9 β -Androst-4-en-3-one, 9,11 β -epoxy-17 β -hydroxy-7,17-
 dimethyl- (6CI, 7CI, 8CI) (CA INDEX NAME)

Absolute stereochemistry.



AB Compds. with anabolic, androgenic, antiestrogenic, gonadotropin-inhibiting, progestational, growth-promoting, anti-fertility, and central nervous system depressant activity were prepared as follows.
 11 β -Hydroxy-17 α -methyltestosterone (5 g.) (CA 50: 7159b), 25 cc. Ac₂O, and 100 mg. p-TsOH (Ts = tosyl) in toluene were refluxed under N 4.5 hrs., the product treated with NaBH₄ 3 days at 5°, followed by reaction with LiAlH₄ gave 1.2 g. 17 α -methyl-5-androstene-3 β ,11 β ,17 β -triol (I), m. 230-5°; [α]_D -68° (dioxane). 11 α -Hydroxy-17-methyltestosterone (1 g.) in pyridine was treated with 1 g. p-TsCl to give 11 α -(p-tolylsulfonyloxy)-17-methyltestosterone, which was refluxed with HCO₂Na 19 hrs. to give 9(11)-dehydro-17-methyltestosterone. I (2 g.) and 12 g. p-quinone in PhMe was refluxed with 2 g. Al(OBu-tert)₃ for 50 min. and chromatographed to give 0.4 g. 11 β -hydroxy-17 α -methyl-6-dehydrotestosterone, m. 246-54°; [α]_D 150° (CHCl₃).

Similarly prepared were 6-dehydro-17-methyltestosterone (II), m. 182-91°; $[\alpha]_D^{21}$ (CHCl₃). Using chloranil, 11 β -hydroxy-testosterone was converted to the 6-dehydro derivative II (2 g.) was treated with a mixture of 0.4 g. Cu₂Cl₂ and 20 cc. 4M MeMgBr in Et₂O in tetrahydrofuran for 4 hrs. and the product chromatographed to give 1 g. of a mixture of the 7-epimers of 7,17-dimethyltestosterone, m. 120-40°; $[\alpha]_D^{55}$ (CHCl₃). Separation of the epimers was effected by recrystn. and reaction with chloranil to give the 7 α -epimer, m. 163-5°, and the 7 β -epimer, m. 127-9°. Similarly prepared were the 7-epimers of 7,17-dimethyl-11 β -hydroxytestosterone, m. 218-24°, and separation as before gave the 7 β -epimer, m. 242-6° (decomposition); $[\alpha]_D^{105}$ (CHCl₃); and by reaction with chloranil to give a residue, 7,17-dimethyl-11 β -hydroxy-6-dehydrotestosterone, m. 242-4°; $[\alpha]_D^{310}$ (CHCl₃), and the 7 α -epimer, m. 225-30°; and 7 α ,17-dimethyl-9(11)-dehydrotestosterone, m. 172-6° [obtained from 7 α ,17 α -dimethyl-11 α -hydroxytestosterone, m. 230-4.5°; $[\alpha]_D^{81}$ (CHCl₃)].

7 α ,17 α -Dimethyltestosterone (8 g.), 8 g. Hg, 6.5 cc. HOAc, 5 g. SeO₂, and 300 cc. tert-BuOH was refluxed under N for 4 hrs. to give, after chromatog., 1-dehydro-7 α ,17 α -dimethyltestosterone, m. 153-6°; $[\alpha]_D^{-6}$ (CHCl₃). 7-Methyl-11 β -hydroxytestosterone (III) (1 g.) was acetylated to give the 17-acetate. III (0.3 g.) in benzene was stirred with 0.3 cc. BzCl and 0.3 cc. pyridine for 17 hrs. at 25° to give the 17-benzoate. This compound (1.5 g.) in 80 cc. HOAc was oxidized with 0.74 g. CrO₃ to give 7-methyl-11-oxotestosterone 17-benzoate. Similarly prepared was 7-methyl-11-oxotestosterone 17-acetate. 7-Methyl-11-oxotestosterone 17-propionate (1 g.) in 50 cc. N alc. KOH containing 3 cc. H₂O was refluxed 0.5 hr. to give 7-methyl-11-oxotestosterone. III (2.5 g.), 250 cc. C₆H₆, 200 cc. Et₂O, 100 cc. concentrated HCl, and 100 cc. H₂O was refluxed 18 hrs. to give 17-methyl-9(11)-dehydrotestosterone (IV). IV (250 mg.) in C₆H₆ was converted to the 17-propionate (V). Similarly prepared was the 17-(β -cyclopentyl-propionate) derivative of IV. V (2 g.) in Me₂CO was cooled to 15° and treated with 2 g. N-bromoacetamide in H₂O, followed by 10 cc. 0.8N HClO₄ to give 7-methyl-9 α -bromo-11 β -hydroxytestosterone 17-propionate (VI). Similarly prepared were 7-methyl-9 α -chloro-11 β -hydroxytestosterone 17-propionate, and 7,17-dimethyl 9 α -bromo-11 β -hydroxytestosterone. VI (1.36 g.) in MeOH was titrated with 0.1N aqueous NaOH to give 7-methyl-9 β ,11 β -epoxytestosterone 17-propionate (VII). Similarly prepared was 7,17-dimethyl-9 β ,11 β -epoxytestosterone. VII (1.13 g.) in CHCl₃ was treated with HF in CHCl₃ at -15° to give 7-methyl-9 α -fluoro-11 β -hydroxytestosterone 17-propionate. This compound (0.779 g.) in HOAc was treated with 0.37 g. CrO₃ in HOAc to give 7-methyl-9 α -fluoro-11-oxotestosterone 17-propionate, which in turn was treated with alc. KOH to give 7-methyl-9 α -fluoro-11-oxotestosterone.

6-Dehydro-19-nortestosterone 17-acetate (3 g.) was treated with 3M MeMgBr and 0.4 g. Cu₂Br₂ to give 7 α -methyl-19-nortestosterone 17-acetate, m. 111-14°; $[\alpha]_D^{48}$ (CHCl₃). This product was deacetylated with aqueous K₂CO₃ to give 7 α -methyl-19-nortestosterone, m. 145-6°; $[\alpha]_D^{55}$ (CHCl₃). This compound (1.4 g.) was oxidized with CrO₃ to give 7 α -methyl-19-nor-4-androstene-3,17-dione, m. 201-4°; and the product (10 mg.) in MeOH was treated with pyrrolidine to give 7 α -methyl-19-nor-4-androstene-3,17-dione 3-pyrrolidinyl enamine (VIII), m. 151-60°. VII (0.5 g.) was treated 5 hrs. with NaC.tplbond.CH in xylene to give 0.161 g. 7 α -methyl-17 α -ethynyl-19-nortestosterone (IX), m. 197-9.5°. Also prepared was the 17-acetate. IX was hydrogenated over Pd/C to give 17 α -ethyl-7 α -methyl-19-nortestosterone, m.

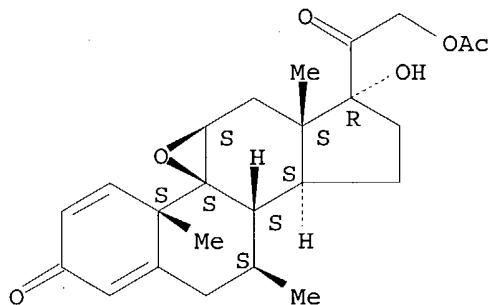
138-9°. VIII (2.75 g.) was reacted with 3M MeMgBr to give 7 α ,17 α -dimethyl-19-nortestosterone (X) which was then treated with *Rhizopus nigricans* ATCC 6227b to give 7 α ,17 α -dimethyl-11 α -hydroxy-19-nortestosterone (XI). X was similarly treated with *Cunninghamella blakesleeana* ATCC 8688b to give the 11 β -isomer of XI. CrO₃-HOAc converted XI to 7 α ,17 α -dimethyl-11-oxo-19-nortestosterone. To 1.6 g. 7 α -methyl-11 β -hydroxy-19-nortestosterone in PhMe and cyclohexanone was added 1.5 g. Al(OBu-tert)₃ to give 7 α -methyl-11 β -hydroxy-19-nor-4-androstene-3,17-dione. 7 α -Methyltestosterone (20 g.) was treated with 20 g. Na₂Cr₂O₇ in HOAc to give 15.6 g. 7 α -methyl-4-androstene-3,17-dione, m. 194-6°; [α]_D 196° (CHCl₃). The product was dissolved in hot MeOH and treated under N with pyrrolidine to give the 3-pyrrolidyl enamine, m. 199-205° (decomposition); [α]_D -190° (pyridine). The compound thus prepared was treated with NaC.tplbond.CH as before to give 7 α -methyl-17 α -ethynyltestosterone, m. 191-3°; [α]_D 41° (CHCl₃). Hydrogenation converted the latter product to 7 α -methyl-17 α -ethyltestosterone, m. 140.5-3.0°. This compound was treated to give the 17-propionate. Uv and ir spectral data are given for the compds.

L8 ANSWER 37 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1963:66717 CAPLUS
DOCUMENT NUMBER: 58:66717
ORIGINAL REFERENCE NO.: 58:11449g-h,11450a-e
TITLE: **Steroids**
PATENT ASSIGNEE(S): Upjohn Co.
SOURCE: 19 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 898492		19620614	GB	
FR 1430064			FR	
PRIORITY APPLN. INFO.:			US	19590819
IT 98423-60-0		9 β -Pregna-1,4-diene-3,20-dione, 9,11 β -epoxy-17,21-dihydroxy-7 β -methyl-, 21-acetate (preparation of)		
RN 98423-60-0	CAPLUS			
CN 98423-60-0		9 β -Pregna-1,4-diene-3,20-dione, 9,11 β -epoxy-17,21-dihydroxy-7 β -methyl-, 21-acetate (7CI) (CA INDEX NAME)		

Absolute stereochemistry.



GI For diagram(s), see printed CA Issue.

AB Prepns. of 7-methyl-9 α -halo-11-oxygenated-17 α ,21-dihydroxy-1,4-pregnadiene-3,20-diones and the 21-acylates was described. 7 β -Methyl-9 α -fluoro-11 β ,17 α ,21-trihydroxy-4-pregnene-3,20-dione (1 g.) and 0.5 g. 3-oxobisnor-4-cholen-22-al (I) in 16 ml. HCONMe₂ incubated 72 hrs. at 28° in a broth containing *Septomyxa affinis* and the product chromatographed on Florisil gave 7 β -methyl-9 α -fluoro-11 β ,17 α ,21-trihydroxy-1,4-pregnadiene-3,20-dione (II). The 9 α -chloro analog of II was similarly obtained. Other species also served to introduce the Δ 1-bond. Similar incubation of 1 g. 7 β -methyl-9 α -fluoro-17 α ,21-dihydroxy-4-pregnene-3,11,20-trione with I and the product chromatographed on Florisil gave 7 β -methyl-9 α -fluoro-17 α ,21-dihydroxy-1,4-pregnadiene-3,11,20-trione (III). Similarly the 9 α -chloro analog of III was obtained. 7 α -Methyl-9 α -fluoro-11 β ,17 α ,21-trihydroxy-4-pregnene-3,20-dione similarly afforded 7 α -methyl-9 α -fluoro-11 β ,17 α ,21-trihydroxy-1,4-pregnadiene-3,20-dione (IV). The 9 α -chloro analog of IV was similarly obtained. Likewise 7 α -methyl-9 α -fluoro-17 α ,21-dihydroxy-4-pregnene-3,11,20-trione gave 7 α -methyl-9 α -fluoro-17 α ,21-dihydroxy-1,4-pregnadiene-3,11,20-trione (V). The 9 α -chloro analog of V was also obtained. II (50 mg.) left 21 hrs. at room temperature with C₅H₅N and Ac₂O gave the 21-acetate. The 21-acetate of IV was similarly obtained. III and related **steroids** were similarly acetylated to give the 21-acetate. II left 20 hrs. at room temperature with succinic anhydride and C₅H₅N gave the 21-hemisuccinate. Other steroidal hemisuccinates were similarly prepared. III also afforded the corresponding 21-hemisuccinate and other 21-esters. 7 β -Methyl-9 α -fluoro-11 β ,17 α ,21-trihydroxy-4-pregnene-3,20-dione 21-acetate (100 mg.) in 6 ml. tert-BuOH and 0.55 ml. AcOH heated 24 hrs. at 75° with 30 mg. SeO₂ and the product chromatographed on magnesium silicate gave II diacetate. Other compds. were similarly treated to give III, IV, and V 21-acetates, resp. II 21-acetate (1.1 g.), 1 g. KHCO₃, 100 ml. MeOH, and 15 ml. H₂O stirred 5 hrs. at 25° under N and the product chromatographed gave free II. Other 21-acetates and 21-acylates were similarly converted to the corresponding 21-hydroxy compds. 7 β -Methyl-11 β ,17 α ,21-trihydroxy-1,4-pregnadiene-3,20-dione 21-acetate (1.05 g.) in C₅H₅N treated 15 min. at 5° with 0.517 g. N-bromoacetamide gave 7 β -methyl-17 α -hydroxy-21-acetoxy-1,4,9-(11)-pregnatriene-3,20-dione (VI). VI (1.27 g.) in 19.5 ml. CH₂Cl₂, 38 ml. tert-BuOH, and treated 15 min. with 3 ml. 72% HClO₄ in 22.5 ml. H₂O, followed by 0.55 g. N-bromoacetamide in 9.6 ml. tert-BuOH gave 7 β -methyl-9 α -bromo-11 β ,17 α -dihydroxy-21-acetoxy-1,4-pregnadiene-3,20-dione (VII). VII (1.749 g.), 1.749 g. KOAc, and 50 ml. Me₂CO stirred under reflux 18 hrs. gave 7 β -methyl-9,11 β -epoxy-17 α ,21-dihydroxy-1,4-pregnadiene-3,20-dione 21-acetate (VIII). Other epoxy **steroids** may be similarly prepared. VIII (2.276 g.) in 9 ml. tetrahydrofuran and 28 ml. CH₂Cl₂ left 17 hrs. at 0-5° with 5.2 g. HF, the mixture poured into 500 ml. H₂O and 25 g. NaHCO₃, stirred, extracted with CH₂Cl₂, and the product chromatographed on magnesium silicate gave II acetate. Other related compds. were similarly prepared. II acetate (1.4 g.) in 140 ml. MeOH stirred 5 hrs. with 1.4 g. KHCO₃ in 17.5 ml. H₂O gave II. Other related compds. were similarly hydrolyzed.

L8 ANSWER 38 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1961:93671 CAPLUS
DOCUMENT NUMBER: 55:93671
ORIGINAL REFERENCE NO.: 55:17694e-h
TITLE: 7 β ,17 α -Dimethyl-4,6-androstadien-3-ones
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable

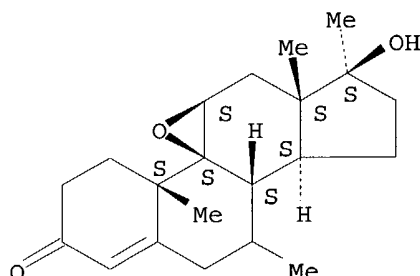
10/608,101

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
	GB 863662		19610322	GB	
IT	17000-71-4		9 β -Androst-4-en-3-one, 9,11 β -epoxy-17 β -hydroxy-7,17-dimethyl-		
			(preparation of)		
RN	17000-71-4	CAPLUS			
CN	9 β -Androst-4-en-3-one, 9,11 β -epoxy-17 β -hydroxy-7,17-dimethyl-	(6CI, 7CI, 8CI)	(CA INDEX NAME)		

Absolute stereochemistry.



AB 3 β ,17 β -Dihydroxy-17 α -methyl-5-androstene 3-acetate in pyridine treated with (F₃CCO)₂O gave the 17-trifluoroacetate (X), m. 116-18°, [α]_D -63° (CHCl₃). Similarly, 3 β ,11 β ,17 β -trihydroxy-17 α -methyl-5-androstene 3-acetate gave the 11 β ,17 β -bis(trifluoroacetate) (XI). X in CCl₄-HOAc-Ac₂O heated with tert-Bu chromate gave 3 β ,17 β -dihydroxy-17 α -methyl-5-androstene-7-one 3-acetate 17-trifluoroacetate (XII). Similarly, XI was oxidized to 3 β , 11 β ,17 β -trihydroxy-17 α -methyl-5-androstene-7-one 3-acetate 11,17-bis(trifluoroacetate) (XIII). XII with MeLi gave 3 β ,7,17 β -trihydroxy-7,17 α -dimethyl-5-androstene (XIV), converted to 3-acetate, m. 164-73°, and XIII was similarly converted to 3 β ,7,11 β ,17 β -tetrahydroxy-7,17 α -dimethyl-5-androstene (XV) and 3-acetate. XIV heated with Al(OCMe₃)₃ in cyclohexanone gave 7,17 α -dimethyl-17 β -hydroxy-4,6-androstadien-3-one (XVI), m. 91-102° (aqueous EtOH), [α]_D 196° (CHCl₃), and XV was similarly converted to 7,17 α -dimethyl-11 β ,17 β -dihydroxy-4,6-androstadien-3-one (XVII). XVII with Na₂Cr₂O₇·2H₂O in HOAc gave 7,17 α -dimethyl-17 β -hydroxy-4,6-androstadiene-3,11-dione (XVIII). XVI with Li in liquid NH₃ gave 7 β ,17 α -dimethyl-17 β -hydroxy-4-androstene-3-one, m. 127-9° (Me₂CO-C₆H₁₄), [α]_D 57° (CHCl₃). The 6,7-double bonds of XVII and XVIII are similarly saturated. The new 7-Me **steroids** are primarily useful as anabolic agents.

=> log y

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

208.88

364.93

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

10/608,101

CA SUBSCRIBER PRICE

-27.93

-27.93

STN INTERNATIONAL LOGOFF AT 18:35:20 ON 16 AUG 2004